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SURGICAL JUDGMENT.*

By J. M. T. Finney, M. D.,

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"Life is short, art is long, experience fallacious, judgment difficult." With the pregnant aphorisms of the illustrious Father of Medicine, every member of this Society is doubtless quite familiar. Fruitful with suggestion, they, along with other of his writings which have come down to us, merit frequent reading, and will richly repay careful study. Even in this twentieth century of advanced knowledge and boasted scientific achievement, a close acquaintanceship with them will stimulate thought and action to higher purpose and to greater endeavor. Indeed, in view of the indifferent character of much of the work that is still being done, of many of the doctrines that are still being taught, of much of the literature with which the medical press teems (to use a mixed metaphor), "half baked" and crude as much of it is, and yet, nevertheless, often stated in terms of Delphic cock sureness—in view of all this, let me repeat, it would appear that the sage aphorisms of the great Hippocrates that have to do with the fallaciousness of experience and the difficulty of judgment, acquire a new significance and apply to our day and generation with peculiar force and meaning.

It has seemed to the writer, therefore, when reviewing the various topics appropriate for consideration in an address such as this, that it might be worth while upon this occasion to depart somewhat from the conventional, and to attempt to analyze, imperfectly though he may, wherein, more especially in the domain of surgery, lies the great difficulty in the way of the attainment of sound and correct judgment, and in what consists the fallacy of experience.

This is a difficult task which we have set ourselves, because it will be at once apparent that judgment and experience are very closely associated and interdependent the one upon the other, and that in the consideration of each one separately, and in their several relations one with the other, there are many different factors to be borne in mind, the relative measure of importance of which, it will be found impossible accurately to determine.

* Presidential address read before The Southern Surgical and Gynecological Association, December 18, 1912, Old Point Comfort, Va.

So far as experience is concerned, it will be readily admitted that the fallacy to which Hippocrates has reference must, from the nature of the case, be inherent. It lies in the improper interpretation of certain phenomena which, from time to time, have come under observation. Furthermore, there is also the liability to error in the correctness of the observations themselves, and, not only this, but there is additional opportunity for error in the fact that these experiences, which must of necessity be recurrent in character (obviously they cannot all happen at once), must be recorded either in the mind of the observer or upon paper, or by other mechanical device, for temporary or permanent record. To err is human! It would seem, therefore, unnecessary to repeat what must be apparent to all, namely, that the possibility of error, common to everyone of these phases, is very real, nay, more than this; owing to the imperfection of our sense perceptions, of all of our mental faculties, of our so-called instruments of precision, of our records, there must be somewhere the absolute certainty of error. It is simply a question then as to how relatively great that error will be, and not as to whether or not it will exist at all. Since then, as we have seen, experience is founded upon repeated observations of certain phenomena, and observation of these various phenomena is made through the senses, and record must in some way or other be made of these observations for subsequent reference, and then by processes of the mind, they must be rightly interpreted in order to form the bases of correct judgment, it can readily be seen that in this interchange, abundant opportunity for error will be afforded.

Let us pursue this line of reasoning a little further. Since these various stages, through which experience must necessarily pass before it can express itself in terms of definite action, are so prone to error, and since in so many important decisions experience is looked to for guidance, and since it so largely influences our judgment and actions in the domain of surgery, as it does in all other affairs of life, and since it often, quite unconsciously perhaps, plays such an important rôle in controlling and directing our impulses, it would appear to be of the utmost importance to consider this problem from a practical standpoint, and to point out, if possible, some way in which improvement along these lines can be made, and our accumulated experiences, an extremely valuable asset when properly interpreted and utilized, rendered less liable to error. This is the purpose of this address. The writer, even if he were able to do so intelligently, has no desire to invade the domain of psychology, or to launch into a discussion of abstruse philosophical subjects which may possibly be suggested by the topic chosen, but which would be distinctly out of place upon an occasion such as this.

The practical question suggested by this discussion which concerns every one of us, and not only us, but our patients as well, is this, "Is there any way in which this liability to error can be materially reduced, and our experiences, vast and varied as they are, rendered a safer guide to our judgment?" Fortunately for all concerned, to this query an affirmative answer can be given. Many, indeed all, of the processes involved, are capable of development and improvement. In other words, we are at once confronted with the problem of education, medical education, in some of its manifold forms, and when I use the term "medical education," I do not use it in any restricted sense. I do not have in mind simply the four years that are ordinarily spent in the medical school, and the year or two in the hospital, for are we not, all of us, at any rate those who will, learning all the time, being educated continually, led out, as the word implies, into larger fields, with an ever-widening horizon; with attractive vistas opening up here and there, beckoning us on and inviting us to enter into other spheres of greater opportunity and usefulness?

It is not our intention, however, to discuss the general question of medical education, further than to indicate, if possible, certain ways in which it may have a distinct bearing upon the subject under discussion. To do more than this would be foreign to our purpose and would lead us too far afield.

It will be readily admitted, I believe, that the physician above all others, is the man whose education should be broad and complete, for to him are entrusted the lives of his fellowmen, and inexperienced physicians, young or old, without adequate preliminary and professional training, should not be permitted to practise so serious a profession. Unfortunately, however, for one reason or another, such permission is granted far too easily at the present time. The fault lies partly with the public in not only permitting but, to a certain extent, encouraging the ignoramus and the charlatan. It would go a long way toward the eradication of this evil if the public would exercise more care and discrimination in the selection of medical men, especially surgeons. The true, well qualified physician, and the self-styled doctor do not and ought not to look alike. But the blame for this deplorable condition of affairs lies chiefly with the profession itself, for it is a lamentable fact that medical education and ideals in this country are low, lower, perhaps, than in other civilized countries. The reason for this is because our medical colleges are, on the whole, so far below the standard set by the rest of the civilized world that it shames us to make a comparison. These facts have been known long and deplored bitterly by the more enlightened members of the profession, but the investigations of the American Medical Association covering a period of several years, and the exhaustive work of Mr. Abraham Flexner of the Carnegie Foundation recently published, no longer leaves the public any valid excuse for their ignorance of or apathy toward the prevailing conditions. As a result of the effect produced by this report, a considerable number of low-grade medical colleges throughout the country have been compelled to close their doors. In this connection let me quote from the late Dr. M. H. Richardson, an honored Fellow of this Society, a man who was himself the personification of the best type of surgeon, and who represented the highest ideals in the profession; he says, "The task before me is a serious criticism of what is going on in every community. There is to my mind no doubt whatever that surgery is being practised by those who are incompetent to practise, by those whose education is imperfect, who lack natural aptitude, whose environment is such that they never can gain that personal experience which

alone will really fit them for what surgery means to-day. They are unable to make correct deductions from histories, to predict probable events, to perform operations skilfully, or to manage after treatment."

What a scathing criticism of our beloved profession, and the especial sting in it lies in the fact that it is unfortunately only too true! Let us for a moment consider this question, for it is fundamental to the production of sound judgment, and let it be understood that what is here said is said in no "I am holier than thou" spirit, for every honest man knows that he makes mistakes, both of judgment and execution, and the writer is no exception to this rule.

From the very nature of the case, surgery must be considered as a specialty and the attributes of specialism are insight, knowledge and experience, and their proper application to practice is impossible without thorough comprehension and mastery. This can only be properly done by one who has been trained from his youth up, and who has been thoroughly well grounded in the fundamentals of the science. Unless one knows and thoroughly appreciates the principles concerned in the handling of tissues, in the repair of wounds, in the causes and results of inflammation, in the characteristics and manner of growth of malignant disease, in the principles of physical science involved in the production and reduction of fractures and dislocations, and in a hundred other points of importance, which time would fail us to mention, he cannot ever hope to get a thorough grasp of questions which are vital to the complete understanding and proper management of surgical problems of every-day occurrence.

It has been said that a surgeon, like a poet, is born and not made. Personally, I do not believe that this statement is altogether true. Unquestionably, some individuals are born with a natural aptitude for surgery, a something which has been characterized as the "surgical instinct," and which every teacher can recognize at once as present in varying degrees in the medical students under his care. It is very far from the writer's purpose to belittle in any way the art of surgery which is of very great importance, and which in the hands of some skilled operators certainly has become developed to the highest degree. It must be conceded, nevertheless, that however high a pinnacle the art may occupy, the science of surgery always will overshadow it, and unless one is well grounded in the principles of true scientific surgery, it must degenerate into something of a trade or a sort of slight-of-hand performance.

My honored preceptor, the late Dr. John Homans, of Boston, a man of wide experience and excellent judgment, and possessing in an unusual degree the characteristics and knowledge which we have been endeavoring to describe, remarked upon one occasion, "Any fool can cut off a leg; it takes a surgeon to save one." This very well illustrates the point that I am endeavoring to make. Surgery is not alone an art. There is a wide distinction between operator and surgeon. The day of the barber surgeon is over. "It is a science, founded upon certain fundamental principles, without a thorough knowledge and understanding of which, no man can do his patient or himself justice."

Now what is the application of all this? If our premises are correct, the conclusion is obvious, namely, that no doctor, no matter who, without a thorough surgical training, has the moral right to attempt to make a practice of surgery. He may succeed in doing certain minor operations or even certain major operations well; he may learn to do, mechanically, certain things fairly satisfactorily to his patient and to himself, and he may have a fair percentage of success; but, sooner or later, he will meet his limitations, and in attempting to go beyond these, with his small and imperfect equipment, some of the catastrophes of surgery will happen, and then who pays the price of his ignorance and temerity? Yes, let me repeat, surgery is far too serious a matter to be lightly undertaken by those who are not thoroughly trained in the fundamental principles underlying its proper performance. Right here let me sound a note of warning, and in so doing I do not wish to be misunderstood—the tendency nowadays is toward the multiplication of hospitals, a tendency that is to be encouraged under proper safeguards. With the general proposition that a hospital is the only place in which to be sick, that is, surgically sick, I am in the heartiest accord, provided only that the hospital is under proper management, and that the surgeon, for I am speaking now only of the surgical aspects of the question, is thoroughly competent to handle surgical cases. But what do we see? As a matter of fact, in my own state, and I think that it probably is a correct index of the situation throughout the country, hospitals are multiplying in many of the smaller towns, towns of a few thousand inhabitants, where there are few or no skilled surgeons, and —here is the danger—where the general practitioner, against his better judgment, is tempted to essay the rôle of surgeon. There are two general reasons for this, aside from the undesirability of performing any operation in a private house. In the first place, the responsibility for a surgical operation in a private house is undivided. The surgeon alone is responsible for the good or bad results, whereas in a hospital it is somewhat different. The cause of this is not easily explained, but it is true nevertheless, that in the case of a patient operated upon in a hospital, there is not the same feeling of individual responsibility upon the part of the surgeon held by the community at large, as in the first instance. In the second place, under the cover of the hospital, and in the more or less seclusion of its operating-room, the would-be surgeon is tempted to do things that he would not dare to do under other circumstances. Particularly is this true, and this is no joke, where the operating-room is furnished with all the modern appliances of the up-to-date hospital. I have in mind now a certain beautiful operating-room in a hospital in a small city, a room walled and ceiled with marble, finished with polished brass and shining glass, everything in it of the costliest description. What is the result? It would appear to the uninitiated impossible, in such an hygienic sanctuary, to commit a surgical sin; and yet one constantly sees in that operating-room heinous crimes committed against the most fundamental surgical principles and technique, which ought always to be kept inviolate. And why is this? Because of those who habitually use this room, not one is a trained surgeon; they have, so to speak, just picked it up.

In the gradual evolution of this palpably wrong condition of affairs, the surgeon himself, or more strictly speaking, some surgeons, are not wholly blameless. There is no royal road to surgery. There is no such thing as surgery made easy. There is no trick about it that can be learned in a ten lesson course by watching the manual dexterity of some especially clever operator, and hearing him vociferously declaim against the old accepted principles of the fathers, and the newer scientific or so-called laboratory methods. It is easy to be led by such false gods into believing that anybody can perform a surgical operation, it looks so easy and it seems so simple, as they do it. But do not be misled into the fatal error of supposing that that is all that there is to it. It means a long, hard journey, years of close application and study, of mental and manual training, of observation and investigation in hospital ward and laboratory, before a man can acquire the experience, the insight, the judgment in sufficient degree, to entitle him to the proud distinction of being rightly called a surgeon, and all that it implies. Says Valentine Mott, than whom I know of no one better qualified to judge, "We regard those as surgeons and those alone who have by conscientious devotion to the study of our Science, and the daily habitual discharge of its multifarious duties, acquired that knowledge which renders the mind of the practitioner serene, his judgment sound and hands skilful, while it holds out to the patient rational hope of amended health and prolonged life." (Quoted by Barnesby.)

The remedy for all this is obvious, do not abolish hospitals but restrict the practice of surgery to the trained surgeon. There would then be no further excuse for such books as that which has recently appeared by Barnesby entitled, "Medical Chaos and Crime," much of the contents of which is unfortunately only too true.

There is also a moral side to this question. The inexperienced operator, owing to lack of proper training and insufficient experience, is often necessarily at fault, both as to his judgment and execution. He is attempting to do something that, in the vast majority of cases, he is not competent to do for the reasons above mentioned. He is placing himself in a false position before the community, and is laying himself open to charges, which in the present enlightened condition of the public, and certainly in some parts of the country, it would be difficult for him to disprove. There are those in every community who, stimulated by shyster lawyers of the ambulance-chasing type, are not slow to take advantage of every mistake, or fancied mistake, upon the part of the operator. It is well, therefore, for every doctor, no matter who, before he essays the part of surgeon, to weigh well the responsibilities that are involved. He should be in a position to prove to an intelligent jury that he has given his patient the benefit of skill equal at least to that which can reasonably be expected from the average well-trained surgeon. This, it appears to me, it would be difficult, indeed impossible for the untried operator to do. The thoroughly conscientious man will think twice and and go very slowly before allowing himself to be forced through an error in judgment into this position. Of course, I am not now referring to those cases of emergency surgery which every physician at times is called upon to perform. In these instances, common humanity and surgical instinct demand that the best be done for the patient and that immediately, even to the extent of a capital surgical operation, in order to relieve his suffering, or to save life, pending the arrival of the skilled surgeon. Then, too, this matter of operating by those not prepared for it, tends toward the lowering of moral and ethical standards in other directions. It is a great temptation to do this sometimes, because the vast majority of doctors are dependent for their living upon the returns from their practice, and it frequently means a great deal for a doctor to turn over to the surgeon a good patient, perhaps wealthy and prominent in the community, in which event the surgeon, after the operation, collects a substantial fee, while the doctor too often receives little or no recognition or pecuniary return for his advice and services.

The cure for all this is to come by enforcing the highest standards in medical ethics and in medical education, and it is to be hoped, an added hospital year as a prerequisite to practice.

It is our duty, yours and mine, to see that medical education is limited to those institutions that can and do give proper opportunities to their faculties and students, and who have sufficient backbone to hold both strictly to account. We should also strive to get public sentiment aroused in support of this necessary advance. The signs of the times are fortunately most encouraging, a widespread and intelligent interest is being taken in educational problems. Particularly is this true of medical education, with a resulting increase in moral and material support. Encouraging too is the growing number of medical schools that are fighting, against tremendous odds, to modernize their equipment and methods of instruction, to foster research and idealism, and to turn out only such graduates as any one of us might welcome in case of sickness, and to whom we can cheerfully intrust the future maintenance of the highest medical standards and the progress of medical science and practice.

The point which we have been endeavoring to make clear, and it is the basis of our whole argument, is that education, broad, long-continued, careful, conscientious, comprehensive, thorough, is the foundation of all good, sound surgical judgment, and that without this previous training, there is in truth no such thing.

Says President Hibben, "Our general knowledge serves to illumine the specific portion of it, which is the special object under contemplation."

The close relationship existing between experience and judgment has already been referred to. His accumulated experiences are of value to the surgeon only in so far as they are correctly interpreted. They may become a source of positive harm if they are improperly understood or applied. Indeed the larger the experience that one has had that has been misunderstood or improperly interpreted, the more dangerous does that surgeon become, for his judgment will eventually be so vitiated and warped thereby, that in his mind right may become wrong, and wrong right. This condition of affairs may be observed in almost every phase of life, in politics, in law, in

medicine, even in theology, for what is Christian Science, that bastard offspring of an unholy union between pseudo-science and false religion, what is it, but a false interpretation of certain phenomena, the existence of which is well recognized? It has been well said of it that "What is true in it is not new, and what is new in it is not true." What of the various "isms" with which the history of medicine is punctuated? What of certain political dogmas that have from time to time held temporary sway in our own and in other lands? All founded upon false theories, the result of a misconception, an improper interpretation of facts, real or imaginary. Are our own individual experiences always accurately observed and recorded? Are they properly interpreted? And when transformed into action, mental or physical, are they always wisely governed by judgment, ripe, sound, born of accurate observation, correct record, proper interpretation, sane reasoning? Are they?

Shakespeare whose wonderfully accurate observation entitles him to be heard upon almost any subject, has this to say: "Experience is by industry achieved, and perfected by the swift course of time." How very true! The same idea is in a measure conveyed by the adjective most often employed in describing the individual whose experience is such as to entitle him to be heard, and his judgment to a measure of respect above that of his fellows, namely, "ripe." The surgeon who by his industry in seeking out additional opportunities for observation along all lines pertaining to his profession, by his painstaking accuracy, by his time-consuming thoroughness, by his careful attention to irksome routine and detail, both in examination and record of his cases, and by burning the midnight oil in the study of the recorded experiences of others, and in mature reflection upon those of his own, has at last, his judgment mellowed like ripened fruit, become "perfected by the swift course of time." He it is who has in truth "by industry achieved" experience and a sound judgment.

"In the investigation of any subject concerning which we regard ourselves entitled to a judgment, not only should we seek as wide a range of observation as is possible concerning the facts upon which we found the judgment, but we should acquaint ourselves also with what other men have thought and written upon the subject. This is to be done not that we may slavishly acquiesce in their judgment, but that by a critical examination of all that is known and reported, we may be the better able to defend our own position, or the more reasonably to modify or to abandon it, as the case may be" (Hibben).

What is it that constitutes good surgical judgment? Is it something that is born in a man and not made? Is it a thing that one man has without working for, without trying especially hard to get, and which another cannot acquire, no matter how hard he may try? When present as one sees it now and then in certain individuals developed to a marked degree, how does it manifest itself? Can it always be recognized and defined when present, or is it a quality that can better be understood than described?

Before proceeding to define this particular process of the mind, let us try to analyze it a bit and consider some of its more important characteristics, also some of the aids that may be made use of in its acquisition, as well as some of the more common errors in the way of formulating correct judgment. To begin with then, one of the most important characteristics of judgment may be defined as insight. "By this term, one means some kind of knowledge, but the word has a certain peculiar significance whereby we distinguish what we call insight from knowledge in general. A man knows the names and faces of his acquaintances, but he has some sort of insight into the character of his familiar friends. A physician knows the way to his office where he sees his patients, but if he is a successful doctor, in the highest sense of the term, he has insight into the structure and functions of the human body in health, the nature and laws governing disease, its various manifestations, its causes, methods of prevention and cure. He must have an intimate knowledge of human nature in its varying moods and phases, he must know something of therapeutics and the action of drugs. He must know something of the fundamental sciences of chemistry, physics, bacteriology, biology, physiology and psychology, etc. He must know something of the indications for and the methods of use of the various instruments of precision used in his calling. In short, insight is a name for a special sort and degree of knowledge, that unites a certain breadth of range, a certain intimate acquaintanceship, a certain sureness of grasp, whereby one is brought into near touch with the objects of his insight. It gives us a view of some connected whole of things, of cause and effect. We can only truly gain this insight when our acquaintance with our object is coherent, close and personal. It can never be obtained at second hand; many things can be learned by rote and hearsay, but if you have won insight into your profession, you have won it not without the aid of your own individual experience" (Royce). Yet experience, characterized by Hippocrates as fallacious, and admitted by common consent to be such, is not of itself sufficient to produce insight, unless the coherence, the breadth of range, the ability to properly correlate and interpret are also present. This insight is not always confined to the scholar or to the learned, but may belong to the unlearned as well. Many otherwise, ignorant and unskilled people have won a great deal of insight into the matter that intimately concerns them. Many very erudite and learned people possess little or no practical insight into anything. Why is this? Simply because accurate observation, the proper association of cause and effect, the ability to discriminate between the important and the unimportant, in short, the knowledge that has been gained is in the former case coherent and personal, while in the latter it is vague and impersonal, and cannot therefore, serve any practical purpose. It goes without saying that honesty is fundamental to the production of good judgment. This fact is at once recognized by the laity as well as by the profession. If the slightest suspicion rests upon an individual as to his entire good faith, how quickly and how hopelessly is his opinion upon any matter discredited. How can anyone reach a proper conclusion who has been dishonest in his premises? How easy it is to fall into dishonest ways, not intentionally so, perhaps, not willingly, but nevertheless dishonest! Thought-

lessness, possibly even carelessness as to methods, too much haste in the endeavor to do more than one is able to do properly, lack of thoroughness, neglect to make use of instruments of precision, of advanced knowledge and up-to-date methods, all essentially dishonest practices tend to vitiate one's judgment.

The value of keen and accurate observation cannot be well overestimated. It is the straws that tell which way the wind is blowing, and so it often is in drawing conclusions, or in the matter of judgment as between two possible views or courses of action. The one whose powers of observation are ever on the alert, trained to see the slightest sign, will often almost unconsciously, by a reflex as it were, detect certain differences which to another would be entirely lost or, if noticed, would mean nothing, but to him point with unerring accuracy the way to a correct solution, it may be of a difficult problem. It is well known that now and then in the course of a physical examination the seemingly important facts elicited may tend to mislead, while some at first apparently trivial and unimportant observation, may subsequently prove to be the key to the situation. This is especially true in matters of diagnosis. I am sure we can all recall numerous incidents of this in our own experience.

What, for instance, is the significance of the sudden cessation of pain occurring in the course of an appendicitis, is it a good or bad sign? How about its relation to changes in the pulse rate? What about that suggestion of dimpling in the skin overlying an otherwise harmless appearing tumor of the breast? What is the meaning of the so-called "air-hunger" which may be the first recognizable expression of an unsuspected internal concealed hemorrhage? It is not chance, it is not having one's luck with one that enables one observer to recognize at once these from among the mass of irrelevant matter, as the facts of real import, while to another their true significance is entirely lost.

The faculty of accurate observation can be increased by acquiring the habit of examining everything within the field of vision. We fail to see many things because we fall into the easy way of passing them by without noting their presence or appreciating their significance. It was said of Charles Darwin by his son that "He wished to learn as much as possible from every experiment so that he did not confine himself to observing the single point to which the experiment was directed, and his power of seeing a number of other things was wonderful." (Quoted by Hibben.) The open-eyed vision is the prime requisite for scientific investigation. This faculty can be encouraged and developed in students by their teachers and it can be done, it seems to me, far better than in any other way, by individual instruction and bedside observation. Just here comes in the great benefit of dispensary and ward instruction in small groups, where the student can live, as it were, with the patient, and where the instructor can, man to man, discuss with the individual student the various clinical phenomena as they develop, and give to each single symptom observed its true weight and significance. Didactic lectures and teaching undoubtedly have their place in medical education, they have rendered excellent service in the past, but nothing can take the place of the personal contact, the marked individuality which a real teacher possesses and which is unconsciously and indelibly stamped upon his pupils. What more striking example of the truth of what has just been said than is furnished in our own profession by the great Billroth who for a generation was the leader of surgical thought in Europe, and who himself during this period trained those who subsequently became themselves the heads of the best of the great German clinics. His genius is reflected to-day and may be seen and easily recognized in that one of his illustrious pupils still living, Professor Von Eiselsberg of Vienna, a shining example of the possibility of combining in the same individual the highest scientific attainment, remarkable technical skill, a charming personality and crowning all, a judgment that seems almost inspired, a living, speaking likeness of his great master.

It would appear to the writer that the career and accomplishments of this great teacher are an irrefutable argument in favor of the possibility of developing in students the power of perception, the scientific spirit, the accurate analysis, the clear judgment which makes them masters and leaders of men. For it is inconceivable that it was a mere matter of chance that brought together in his clinic a body of men of superior intellectual and professional attainments, which must of necessity and in spite of rather than because of his influence, rise to the top. Undoubtedly Billroth was an excellent judge of men, and was able to pick out of the crowd as his personal assistants, those of superior ability, and capable of the highest development. This was but an additional evidence of his own good judgment which was so abundantly shown in other ways. What an inspiration and example to all of us, teachers and practitioners as well, to follow and to emulate!

How often one sees reflected in the student the methods of thought and action of the teacher; a pet phrase, a characteristic pose, some particular idiosyncracy which brings to mind immediately and unmistakably some strong personality under whose influence, during the formative period of his life, this particular individual has come. One is often impressed with the widespread influence exerted by the teachings of certain particular schools. Here habits of thought are established in certain well worn grooves which may be handed down from generation to generation, practically unchanged. Methods of action are thus influenced to such a marked degree by precedent and custom, that the wheels of progress may be greatly retarded, and advances, the efficacy and value of which have long since been established, indefinitely delayed. Take, for example, the question of choice of anesthetic and the method of its administration, both in this country and abroad, for the past twenty-five years, and compare methods and results. Progress on both continents has been and is still being delayed, and much unnecessary suffering and discomfort as well as an appreciable percentage of mortality induced, the direct result of too close imitation and too slavish following of discredited precedent, though often the offspring of eminently respectable parentage. How important, then, for teachers as well as schools, for the teachers primarily make the schools, to stand only for the best in everything in the educational world in the

language of the present day political vernacular, to be progressively conservative or conservatively progressive, "to prove all things, to hold fast that which is good."

The exercise of judgment, then, does away with the blind following of precedent. It is at times far better and more courageous to discard old precedent and to create new, founded upon correct observations, whether original or not, upon sound conclusions, whether at variance with preconceived notions or so-called authoritative utterances or not, than blindly to accept and supinely follow an authority, no matter how eminent. In these days of more independent thought and action, authority is not so widely recognized nor so highly respected as formerly. While this present tendency has much to commend it, there are certain evident dangers to be pointed out and avoided. In casting off the old, there is the danger of taking up with new and false gods. Fortunately, for surgeons and patients alike, there seems to be less tendency nowadays, perhaps than formerly, to follow certain fads. The days of reckless and indiscriminate operation upon the pelvic organs of the female, of nephroraphy, of gastroenterostomy, of cholecystectomy, are happily past. The stomach and the gall-bladder are still on the firing line, but the seat of war seems to be gradually shifting to the large bowel and the tonsil. There will probably always be found those whose judgment will be carried away by their enthusiasm for something new, by their eagerness to follow prevailing fashions in surgery as in dress, but it will also be found that the surgical judgment of such is as hobbled and narrow as the up-to-date style in skirts. It is truly wonderful with what facility the Aladdin's lamp of the faddist can, for him at least, instantly convert fancy into fact, and thus render an otherwise valuable member of society, or an association of such, not only of little real value, but it may be a positive menace to the human race. Witness the senseless ravings and false accusations of the various societies of the "anti's," the anti-vaccinationists, the anti-vivisectionists, etc. Nothing is more fatal to sound reasoning, nothing so productive of mental strabismus as the fad and the hobby.

As has already been suggested, judgment is not always the result of logical processes readily apparent. The line of reasoning is not always easy to follow, indeed at times it cannot be followed except by very close study and analysis of the intervening steps. There may be a sort of Sherlock Holmes' method about it, which is not readily understood by the ordinary individual, but which when carefully analyzed will show that the conclusions arrived at are no more than his, the result of happy chance or good luck, but are the inevitable result of close observation, of attention to the minutest detail, of intelligent thought, of sound reasoning. When this is done, the conclusions must inevitably follow, and they will be right or wrong just in so far as these various intellectual processes have been intelligently and correctly carried out. But there are other factors concerned. One must not be misled into thinking that it is a sort of rule of thumb, a sort of picture puzzle, the pieces of which have been cut into all sorts of fancy and bizarre shapes, and that it is simply a question of mechanically fitting them together. Not at all! Here as everywhere else imagination, constructive imagination, is of the greatest help. As could the great Cuvier when given but a single tooth, construct the entire skeleton of a prehistoric animal, so can one in his imagination weave the entire pattern from here and there a few broken and tangled threads, supplying those that are missing, and mending those that are broken, until at last there exists in his mind a picture of the whole, clear, concise, complete, correct. The idealist, the dreamer of dreams, while not always, indeed perhaps rarely of a practical turn, is the one who of all others can penetrate deeper into the unknown, can see further into the mists of uncertainty and doubt, can make lighter the dark places of ignorance and uncertainty with the illuminating power of his imagination. "In this connection, however, attention should be directed to the condition that imagination in order to be really helpful must be at all times in touch with fact. It must represent to the mind not what fancy suggests, but what the known facts necessitate" (Hibben). The unseen is then constructed out of the determining conditions of the seen, otherwise fancy might run riot, and our judgment and hypotheses resulting therefrom, rendered correspondingly wierd and bizarre.

One of the fundamental requisites of good judgment must ever be sanity or what is known as common sense. One never expects from the insane or the foolish an opinion that is really worth anything upon any subject. Unfortunately, however, one need not be an inmate of an asylum for such unfortunates, in order to give occasional expression to opinions or exhibit actions worthy of them. Only too frequently one sees in the medical press articles expressing opinions, making suggestions, even giving advice that one would not ordinarily expect to hear outside the walls of such an institution. It is humiliating to have to admit in such an assemblage as this that some of us, and the writer feels constrained to include himself in this number, are at times guilty not only of giving advice but of performing operations, and in such a manner that in the light of further knowledge, more painstaking examination, more careful consideration, more time taken from a life overcrowded, perhaps, with the humdrum of routine and detail, puts us to shame, and which if we are truly conscientious in our work, effectually prevents any tendency toward the pride and conceit of life. Some people are by nature, perhaps, more sane, more stable, more normal in their mental processes than others. Some people are perfectly sane on some subjects and not upon others. It is extremely difficult at times to distinguish between the sane and the insane, between the sound and the unsound judgment. "Mens sana in corpore sano" is a trite but true saying.

It does not, however, necessarily follow that a sane mind and good judgment will always be found in a healthy body, nor will an unhealthy body necessarily always be found to house an unsound mind. But universal experience bears out the contention that a mind free from the distractions and worries that necessarily attend upon physical infirmities of one sort or another, or from the cares of business is in much better condition to grapple with the manifold problems of disease, of diagnosis and treatment. In our busy lives, filled to the utmost with endeavor to help and relieve others, we are prone to forget

self, a virtue always to be cultivated within reasonable limits, but the trouble with us is that we are apt to go to the limit of our endurance, and frequently beyond. Thus in our praiseworthy efforts to relieve others, and in our very self forgetfulness, we often tend to defeat the end for which we have been striving, namely, to give our patients the very best that is in us in the way of advice and treatment, which are in turn the result of our experience, ripe, wide, wisely interpreted by a brain properly working and which is not already tired out by ceaseless work and worry, and a judgment unwarped and unclouded by the pessimism engendered by a torpid liver, or a disturbed digestion.

There are negative as well as positive qualities that go with good judgment, which if not of such high order perhaps as the others, are nevertheless of great practical importance. In matters involving action, surgical treatment, operative as well as non-operative, it would be difficult to overestimate their value. In this connection, Billroth has written, "Years and experience bring in their train a certain degree of hesitancy." One frequently hears the terms radical and conservative applied to surgery and to surgeons as well as to things political. What is their meaning but that one individual or class of individuals is apt more or less blindly to do certain things under given conditions, while the other group is more likely not to do so. A favorite saying of a well-known surgeon, a man of action, but, at the same time, of unusually good judgment, was, "Nine men out of ten will know what to do under given conditions, but the tenth man will know what not to do, and he is the most valuable man of the ten." The truth of this saying, I am sure, has been demonstrated upon more than one occasion to everyone in this assemblage. The conservative surgeon is one who will take the time and the trouble necessary to observe his patient for a season sufficiently long to enable him to get some sort at least, of a comprehensive and intelligent grasp of the situation, before he is willing to express an opinion that may commit him to a definite line of action, especially when that action involves the performance of a surgical operation, however trivial it may appear. For none knows better than the experienced surgeon what far-reaching possibilities for good or for evil are lurking behind every surgical procedure. There is such a thing, of course, as over-caution which leads to inactivity and hesitation when resolution and action are urgently indicated. There are times in the experience of every surgeon when the exigencies of the case demand most instant and most radical operation, and when this becomes the height of conservatism; for example, certain forms of rapidly spreading infection, fulminating appendicitis, hemorrhage, beginning malignant disease, etc. Undue haste, however, either at the time of the operation, or in the preparation of the case, *i. e.*, operating before the patient is in proper condition, or before one is ready to cope properly with any emergency that may arise, are all evidences of poor judgment, and are equally reprehensible.

The influences working toward the production of errors of judgment, as has already been indicated, are manifold, far too many indeed to attempt to enumerate them all here. Errors of observation, failure to differentiate relevant from irrelevant facts, or to comprehend the whole situation, limited view, mental astigmatism, preconceived ideas, narrow-minded provincialism, human frailties, all of them play a large part in determining the results of our mental processes. We are so often swayed by prejudice. We are apt to be too much influenced by the character or personality of our patients. We so often see that which we wish to see and fail to see that which we do not wish to see; we are prone to twist the facts to suit the theory, rather than the theory to suit the facts. Thus we deceive ourselves. Our reasoning is at times faulty, "Post hoc ergo propter hoc," or "non causa sed pro causa" play far too prominent a part in the formation of our judgments. Our emotions and our passions are given too free a rein. We are so prone to forget that we do not profit as we should by our mistakes. The sacrifice is often for us in vain. As Bacon says, "The human understanding resembles not a dry light, but admits a tincture of the will, and passions which generate their own systems accordingly, for man always believes more readily that which he prefers, his feelings imbue and corrupt his understanding in innumerable and sometimes imperceptible ways." (Quoted by Hibben.) This same author in refrring to the errors of judgment, due to the common frailties of human nature, has aptly styled them "idols." His enumeration is complete and classic and is as follows: "Four species of idols beset the human mind to which for distinction's sake we have assigned names, calling the first, idols of the tribe, that is, those inherent in human nature; the second, idols of the den, that is, those peculiar to each individual; the third, idols of the market, that is, those formed by the reciprocal relations of business and society, between man and man; the fourth, idols of the theatre, that is, those which have crept into men's minds from various dogmas, tradition and superstition, all of which tend to clog the mental processes and vitiate judgment."

From this very imperfect review of some of the more important factors, both positive and negative, which go to make up good judgment or to render difficult its attainment, it will readily be seen that with few exceptions, perhaps, those elements tending toward betterment and enlargement of the character and scope of our judgment are capable of development and improvement, while those idols of the mind, those forces which make for error and which tend to vitiate and render difficult our judgment may, some of them at least, be cast down and destroyed, or are by education and experience largely to be eliminated and their influence thereby markedly diminished.

Judgment is then, after all, a thing that may be, to a certain extent, at least, acquired by every one. It is assuredly better developed in some than in others, partly by divine gift, born with it, if you will, partly by education and experience. None need despair, however, by conscientious, intelligent application and study to develop the essentials and to avoid the errors, of eventually obtaining a fair proportion, at least, of that most to be desired of all qualities that go to make up a surgeon, good judgment which, if we were called upon to define in a few words, our answer would be something like this: The ability to discriminate between important and unimportant facts, between the essential and the non-essential, coupled with the

ability to draw correct conclusions therefrom. Given, as a foundation, a mind endowed by nature with an average amount of intelligence or even a little more, and of that *sine qua non*, common sense; an even disposition tinctured with the milk of human kindness; a keen perception: develop this by education, fundamental, broad, comprehensive, scientific, special; add to this accurate observation; experience "by industry achieved"; a familiarity with the work of others gained through reading and by travel; time taken to properly assimilate all this and rate it at its true value by thought and investigation; a trained hand; insight into this old human nature of ours and some knowledge of her various moods and vagaries; crown this with some of the virtues of The Great Physician, our Master and Teacher, and you have pictured before you the surgeon, fully endowed with that quality which we have but imperfectly described, Surgical Judgment, which when developed as we have seen it in the persons of some of our own teachers and friends, both living and dead, is the noblest work of God.

TESTS FOR HEPATIC FUNCTION AND DISEASE UNDER EXPERIMENTAL CONDITIONS.[1]

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At this time we do not wish to discuss any of the liver functional tests proposed by earlier writers, but desire to call attention very briefly to three tests which may be of value in the study of pathological changes in the liver. We expect to publish in the near future detailed work upon which this abstract is based. A very few cases or experiments will be cited as characteristic examples of any given condition.

Lipase can be shown to be present in the blood plasma or serum of normal animals or human beings in a pretty constant amount. The method is briefly as follows: Four tubes are prepared, each containing 1 cc. plasma or serum diluted with 4 cc. distilled water and .3 cc. toluol to check bacterial activity. To two of the tubes is added .26 cc. ethyl butyrate, the other two serving as controls. The tubes are shaken, corked and placed in an incubator at 38° C. for 18-24 hours. They are then cooled in ice water, three drops of azolitmin added and titrated in pairs to a neutral reaction, using 1/10 normal acid and alkali. The two control tubes usually show the blood alkalinity to be .10 cc. of 1/10 normal acid and the butyrate tubes show the acid production to be .10-.20 cc. above the neutral point. This means that the total *lipolytic activity* is .20 to .30 cc. 1/10 normal solution, that the lipase of the plasma has split up the ethyl butyrate to this extent. We may speak then of a *normal plasma lipase* as .20-.30 cc. (always speaking in terms of tenth normal acid).

We have found that injury of the liver by chloroform, phosphorus, hydrazine, etc., will always cause a rise in plasma lipase. After chloroform anæsthesia of 1 to 2 hours the plasma lipase in dogs will rise as high as 1 to 2 cc. 1/10 normal acid. This rise takes place during the first few hours following the anæsthesia and usually persists during the second and third day following, when repair begins and the lipase falls to normal with recovery. If the animal or person is fatally poisoned the lipase will continue high until death on the fourth or fifth day. We have tested this lipase reaction in various experimental conditions where the liver is injured and find a constant rise of 2-8 times normal activity. We have followed the lipase in human cases and believe this test may be of value in certain groups of cases.

Eclampsia is variously defined, but if we limit the name to those cases showing peripheral hemorrhagic liver necrosis, this test is of the greatest value. We have had the opportunity of testing the blood from several cases in the service of Dr. J. W. Williams. In a recent case the blood was obtained during the first series of convulsions and showed 1.-1.15 cc. lipase which pointed certainly to liver injury. The patient died the following day with all characteristic symptoms and autopsy (3883) showed hemorrhagic portal liver necroses as usual. The plasma obtained shortly after death showed even higher lipase readings (1.10-1.40 cc.). In pernicious vomiting of pregnancy and uremia with convulsions, the lipase shows normal readings.

Jaundice may show a slight rise in lipase, but often a normal content and obstructive jaundice of months duration may show a low lipase. Pneumonia, peritonitis, leukæmias and various infections may show a rise in lipase to double normal or even more, but this will rarely confuse one. It is probable that in such conditions the excess of lipase is referable to liver changes, either liver injury or liver stimulation due to cell-split products circulating in the blood. *Yellow atrophy* of the liver surely will show a high lipase reading and in the *early stages* of liver cirrhosis the test will be of value and interest. *Liver cirrhosis* in the late stages may show a low lipase reading unless complicated with some liver necrosis.

Fibrinogen is normally present in blood plasma: in normal human beings it amounts to .300 to .400 gms. per 100 cc. plasma. In dogs it fluctuates more widely (.200 to .500 gms.). It has been shown in this laboratory (Whipple and Hurwitz[2]) that fibrinogen may fluctuate with liver injury, falling to a low level at the time of injury and returning above normal during the repair which rapidly follows. It may drop to such a low level as to be the cause of hemorrhage or a hemorrhagic tendency, because the blood clots are too soft to check hemorrhage. This explains the hemorrhages of yellow atrophy of the liver, phosphorus and chloroform poisoning, yellow fever, etc. In chronic liver cirrhosis the fibrinogen is often below

[1] Presented before the Association of American Physicians, Washington, May 7, 1913.

[2] Whipple and Hurwitz: J. Exp. M. 1911, XIII-136.

normal and at times so low as to favor hemorrhage. In such conditions the fibrinogen estimation may give valuable information. When it falls to a low level it invariably indicates a grave condition and advanced liver injury, acute or chronic.

A rough estimation of the fibrinogen is possible by causing a little oxalate plasma to clot on adding calcium. The toughness of the clot indicates in a general way the amount of fibrinogen and with some experience one can say whether the fibrinogen is much decreased in amount. The clear oxalate plasma may be heated at 59° C. for 20 minutes, the fibrinogen which is precipitated, collected by centrifugalization, washed with cold and hot water, dried with alcohol and washed with ether. This precipitate is then collected in a weighed Gooch crucible, dried at 120° C. and weighed. Twenty cubic centimeters of plasma are best used for each determination. This heat method is quite accurate except when the fibrinogen is very low; under these conditions it gives too low an amount and, if possible the plasma should be clotted with fresh serum and the fibrin weighed after washing, etc.

In certain cases of hepatic cirrhosis we have reported a very low fibrinogen index (Whipple[2])—a drop to .050 gm. or even less. This is not an invariable finding in this disease, but when present is of the gravest prognostic import.

In human cases of fatal late chloroform poisoning the fibrinogen during the last two days of the intoxication may drop to .048 gm. and finally to .034 gm. per 100 cc. plasma (autopsy 3726). When the liver is exposed to minor injuries it may respond with an over-production of fibrinogen, which may rise even to 1 gm. per 100 cc. plasma. This minor injury may be looked upon as a stimulus and the high fibrinogen content found in pneumonia, septicæmia, peritonitis, etc., can be explained by the action of certain substances upon the liver epithelium. These substances may be derived from disintegration of the body cells or foreign cells and when very abundant may be able to cause degeneration and even liver cell necrosis, but in lesser amounts may be imagined to have a stimulating action (or irritative effect) upon the liver.

Phenoltetrachlorphthalein is a drug which is excreted by the liver into the bile. Abel and Rowntree[4] reported a study of this drug in connection with work on subcutaneous purgatives. Rowntree,[5] who was familiar with the characteristics of phenoltetrachlorphthalein and had established the normal excretion in dogs with biliary fistulæ, suggested that we use the drug in our work with abnormal hepatic conditions. The drug which was used had been supplied to Rowntree by Professor Orndorff of Cornell University. A preliminary series of experiments on dogs, whose livers had been acutely injured by various means, showed that there was a remarkable decrease in phthalein output during the period of liver injury. Rowntree, Hurwitz and Bloomfield then proceeded to apply the test to patients in the wards, since which time the experimental and clinical work has been going on side by side with concordant findings. More careful experiments show that there is a very striking parallelism between the amount of liver injury and the output of phthalein. The drug was given subcutaneously in the first experiments, but it was found that the *intravenous* injection of the sodium salt offered many advantages over the oil method.

The procedure which gives best results in the experimental work may be outlined as follows: Female dogs are used when possible to facilitate catheterization and are given .100 gm. phthalein when weighing between 10 and 20 lbs.—.200 gms. when over 20 lbs. The solution is injected intravenously, given usually in the forenoon. The dog is then given water (200-300 cc.) by stomach tube to promote diuresis. After a period of five or six hours the urine is collected and a purge given, usually magnesium sulphate and croton oil in sufficient amounts to give several semi-fluid stools. The feces are collected the next morning and experience shows that no phthalein can be obtained by subsequent purgation. It is important to obtain brisk purgation, as it is known (Abel and Rowntree) that the drug is absorbed from the large intestine and must be swept out rapidly to give a uniform result. Delay of purgation for 24 hours will drop the phthalein output from normal (40-50 per cent) to 30 per cent or even a little lower.

The method of extracting the feces is relatively simple and not time consuming. The total feces are diluted to 1 or 2 liters as may be necessary in collection from the metabolism cages. The mixture is made alkaline with sodium hydroxide (5-10 cc. of a 40 per cent solution) and shaken until a good uniform mixture is obtained. One-tenth of this is taken and diluted to 500 cc. with water, 3 to 4 cc. of 40 per cent sodium hydroxide added and the mixture thoroughly shaken. Of this second solution are taken 100 cc. for precipitation with basic lead acetate (5 cc. of a saturated solution). After a few seconds a curdy precipitate comes down and the solution is then made up to 200 cc. with water containing 4 cc. of sodium hydrate (40 per cent). On standing the supernatant fluid shows a clear phthalein color and with filtration gives a solution which can be read directly in a colorimeter[6] against a standard solution—10 mg. phthalein to the liter.

This procedure in our hands gives a very uniform phthalein output in the feces of normal dogs, 35-50 per cent with .100 gm. injections and 40-55 per cent with .200 gm doses. The same dog may show fluctuations within these limits depending in part upon purgation and collection of feces. The drug given in these doses does not come through in the urine of a normal dog. Phthalein given by stomach and collected in the feces in the usual way will average 60-65 per cent, showing the amount of drug which is lost through contact with the intestinal mucosa and collection of the feces. When the phthalein is added to large amounts of feces it can be recovered completely (97-100 per cent) by the method outlined above.

This shows that only 10-15 per cent phthalein is lost from the time the phthalein is injected intravenously until it is poured out by the liver in the bile into the duodenum. This indicates a remarkable degree of secretory activity and specificity of the liver epithelium.

[2] Whipple: Arch. Int. M. 1912, IX-365.

[4] Abel and Rowntree: J. Pharm. and Exp. Therap., 1909, I-231.

[5] Rowntree: J. Am. A. Asso., 1910, LIV-344.

[6] R. and G. modification of the Autenreith-Konigsberger colorimeter, which reads directly in per cent.

When *liver injury* is produced by chloroform, phosphorus, hydrazine or other agents there is a drop in feces output to 20 per cent, 10 per cent or even a mere trace, depending on the extent of the liver injury, and the *phthalein* now comes out in the *urine* ½-4 per cent. The mechanism of liver repair is familiar and with this return to normal the phthlein output comes slowly back to normal. This is illustrated by a simple type experiment.

Dog 12-48.—Strong female fox terrier, 14 pounds.

April 3, 12 m. Phthalein .100 gm. intravenously. 5 p. m. Urine. Phthalein negative. Purged.

April 4, a. m. Feces collected. Phthalein 47 per cent.

April 8, 11 a. m. *Chloroform anæsthesia 1¾ hours.* At end of anæsthesia given *phthalein* .100 gm. intravenously. 5 p. m. Vomitus and urine. Phthalein 12 per cent.

April 9. No feces. Dog vomits purges.

April 10, 10 a. m. Fluid feces. Phthalein 7-9 per cent. 12 m. Urine contains bile pigments. Phthalein negative.

April 10, 3 p. m. Phthalein .100 gm. intravenously. 5 p. m. Urine 100 cc. Phthalein 1½ per cent. 7 p. m. Urine 100 cc. Phthalein 1 per cent. 9 p. m. Urine and vomitus. Phthalein 1½ per cent.

April 11, 9 a. m. Urine plus vomitus. Phthalein 2 per cent. 4 a. m. Abundant feces. Phthalein 25 per cent.

April 12. Dog is improving rapidly and eats well. Weighs 12½ pounds.

April 15, 1 p. m. Phthalein .100 gm. intravenously. 4 p. m. Urine. Pthalein 0.1 per cent. Purged.

April 16, 10 a. m. Feces abundant. Phthalein 45 per cent.

The average amount of injury done to a dog's liver by two hours chloroform anæsthesia is a central necrosis involving about two-fifths of the parenchyma of each lobule. We may assume some such injury in the above case and the prompt drop to less than half phthalein output with return to normal within a week is to be expected from the knowledge of the process of repair following such an injury (Whipple and Sperry[7]). It is possible to injure the liver so severely that the phthalein output may drop almost to zero, and in a majority of such cases the injury will lead to the death of the animal. The following experiment shows a severe liver injury followed by recovery, the phthalein falling about to zero:

Dog 12-90.—Small mongrel male, weight 11 pounds.

April 10, 3 p. m. Phthalein .100 gm. intravenously.

April 11, 10 a. m. Feces abundant. Phthalein 43 per cent.

April 14. *Hydrazine* sulphate .100 gm. given subcutaneously.

April 15, 1 p. m. Phthalein .100 gm. intravenously. Hydrazine sulphate (2d dose) .100 gm. subcutaneously. Weight 10 pounds. 5 p. m. Urine. Phthalein 1½ per cent. Vomited, purged.

April 16, 9 a. m. No feces. Vomits purges. Dog looks very sick. Urine and vomitus. Phthalein 4 per cent. 4 p. m. Feces small amount. Phthalein mere trace (2 per cent).

April 17. Jaundice is evident in skin. Dog very dull. 11 a. m. One soft stool. *Phthalein mere trace.*

April 18, 10 a. m. Dog slightly better. Urine shows large amount of bile and faint cloud of albumin. Weight 8½ pounds. 2 p. m. Phthalein .100 gm. intravenously.

April 19, 9 a. m. Cage urine. Phthalein (2 per cent), one fluid stool. Phthalein 8 per cent.

April 22, 12 m. Urine free from bile and albumin. Dog is very much better. Phthalein .100 gm. intravenously. Weight 9 pounds. 5 p. m. Urine. Phthalein 2 per cent. Purged.

April 23, 10 a. m. Feces abundant. Phthalein 35 per cent.

It is obvious that this test can be of little value in *obstructive jaundice,* but it is interesting that little if any of the drug will escape in the urine. When the phthalein is given shortly after ligation of the common bile duct—the same or following day—the urine will show but a trace of phthalein. When the obstruction has been present days or weeks the phthalein will appear in the urine (1-2 per cent) and we believe in each case this is dependent upon true liver injury. When the phthalein remains in contact with the body tissues for 24-48 hours in obstructive jaundice, it is changed to some substance which is not recognizable, but traces can be found in the gall bladder three to six days after a phthalein injection in obstructive jaundice. The drug is not secreted by the intestinal mucosa and in complete obstructive jaundice there is never a trace of phthalein in the feces.

Passive congestion of the liver cannot be produced in dogs to the extreme degree seen in human cases with broken cardiac compensation. However, it is possible to produce passive congestion of the abdominal viscera by means of stitches placed in the vena cava inferior just above the diaphragm, narrowing the lumen to 1 or 2 mm. in diameter (McClure). Such animals develop extreme ascites, collateral circulation, enlarged spleen, etc., and they show a slight decrease in liver excretion of phthalein with no escape in the urine.

The Eck fistula produces a liver which has a scanty blood supply, chiefly arterial, and the liver undergoes a slow atrophy with some fatty change in the early stages. These dogs show a decrease in phthalein output (20-30 per cent) and the urine contains 0.5-3 per cent phthalein. This indicates a certain degree of liver insufficiency and liver injury. It is interesting that an Eck fistula dog living over a year has an output which has returned practically to normal and only traces of phthalein in the urine, indicating that the liver has regained its functional balance. The clinical features of these animals support this interpretation.

It is clear that phenoltetrachlorphthalein gives promise as a functional liver test. It is excreted in the bile through activity of the liver epithelium and not the bile duct epithelium. Any agent which injures the liver parenchyma or interferes with its functional activity will cause a drop in phthalein output in the feces. Acute liver injury also is associated with an escape of phthalein in the urine, we believe due to a modification of the phthalein through the agency of the injured liver cells, so that it passes through the renal epithelium. Clinical material is being studied by Rowntree, Hurwitz and Bloomfield. The details of drug preparation, injection and collection will appear shortly with a report on these clinical studies. It may be said that the findings in clinical cases which have been supported by autopsy or exploration are in harmony with the experimental observations.

It is probable that with accumulated experience in the interpretation of the varied findings in these three tests, we may be able to define more and more accurately the anatomical and functional abnormalities of the liver.

[7] Whipple and Sperry: Johns Hopkins Hosp. Bull., 1909, XX-278.

MULTIPLE CONGENITAL OSTEOCHONDROMATA WITH DEGENERATION OF CRANIAL NERVES AND MUSCULAR DYSTROPHY.

REPORT OF CASE.

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Congenital exostoses and enchondromata are among the rarer skeletal anomalies and have attracted much attention from the clinical observer and pathologist. The literature of the subject is voluminous and has been satisfactorily reviewed by others (Schmidt, Frangenheim). The writer will therefore limit himself to a brief statement of what is generally accepted as to the occurrence and histogenesis of the condition with a description of a case with unusual associated features.

While very few observations on the new-born are recorded, such cases have been described by Murchison and Syme, Vix, Koester, Myers, and others. And there is much reason to accept the view that these tumors are truly congenital and due to abnormal anlage in the intermediary cartilages (v. Bergmann).

The anomaly is, in many cases, clearly hereditary, and the heredity may be immediate from parent to child, or miss a generation. Likewise, an individual with exostosis may have descendants, with enchondroma, or vice versa. Or, either type may show mixed heredity in the descendants. The incidence is greatly preponderant in the male members of such families.

The causes of the anomalous development are still obscure. Several authors have noted thyroid hypoplasia, cystic goitre, or Basedow's disease in their cases. Poor development of the mental and sexual functions has also been remarked. Intermarriage of relatives has been suggested by some authors as a possible factor.

The exostoses are more common on the long bones, those of the lower extremities being more frequently involved than the bones of the arms. Small exostoses are often found on the ribs, especially near their heads. The feet and hands, as a rule, show few exostoses, while the pure enchondromata are most frequent on these parts. In general, the distribution of the growths is symmetrical, although exceptions occur in which one-half of the body, or one limb, is involved. The cranial bones of periosteal origin are free from this type of anomaly, but exostoses have been found at the sutures.

The characteristic deformities produced are: distortion and shortening of the long bones, with dwarfism, the trunk being better developed than the extremities. The sites of election for the tumors on the long bones are metaphysis, epiphysis, and diaphysis in order of frequency. The size of the exostoses varies from a few millimeters to many centimeters in diameter. In the forearm and leg the bones are often bridged by exostotic processes.

Bowing of the radius, with or without dislocation of the elbow, is quite frequent, due to the overgrowth of the radius stimulated by the tumor at the epiphysis. Bursæ at the outer portion of the tumors are common and may be large and contain floating bodies.

The cartilaginous covering of the exostoses is irregularly distributed and disappears during puberty, when growth of the tumor ceases. Later some absorption may take place; in a few instances the tumors have entirely disappeared. The structure, histologically, is very like that of normal bone. Primary necrosis and large areas of cystic degeneration are quite uncommon. Sarcomatous metamorphosis has been observed very rarely.

The tumors themselves are, for the most part, harmless, and they are not painful. But they may produce grave symptoms from pressure on contiguous blood vessels and nerve trunks. The skin over the exostosis may become necrotic from pressure and lead to a severe local abscess or a general infection. In women the presence of exostoses in the pelvis may interfere with child-bearing. Exostoses may hamper the movement in important joints.

Very little is known of the association of other congenital anomalies with exostosis. Several cases of extensive spinal cord lesions have been noted (Oberndorf), and some writers assert that anterior horn cell degeneration in the cord causes trophic changes in the bones, leading to exostosis.

The patient, W. K., white, 22, single, teamster, was admitted to the City Hospital, July 20, 1912, complaining of weakness of the legs.

On account of absolute deafness, the history was difficult to obtain, and imperfect.

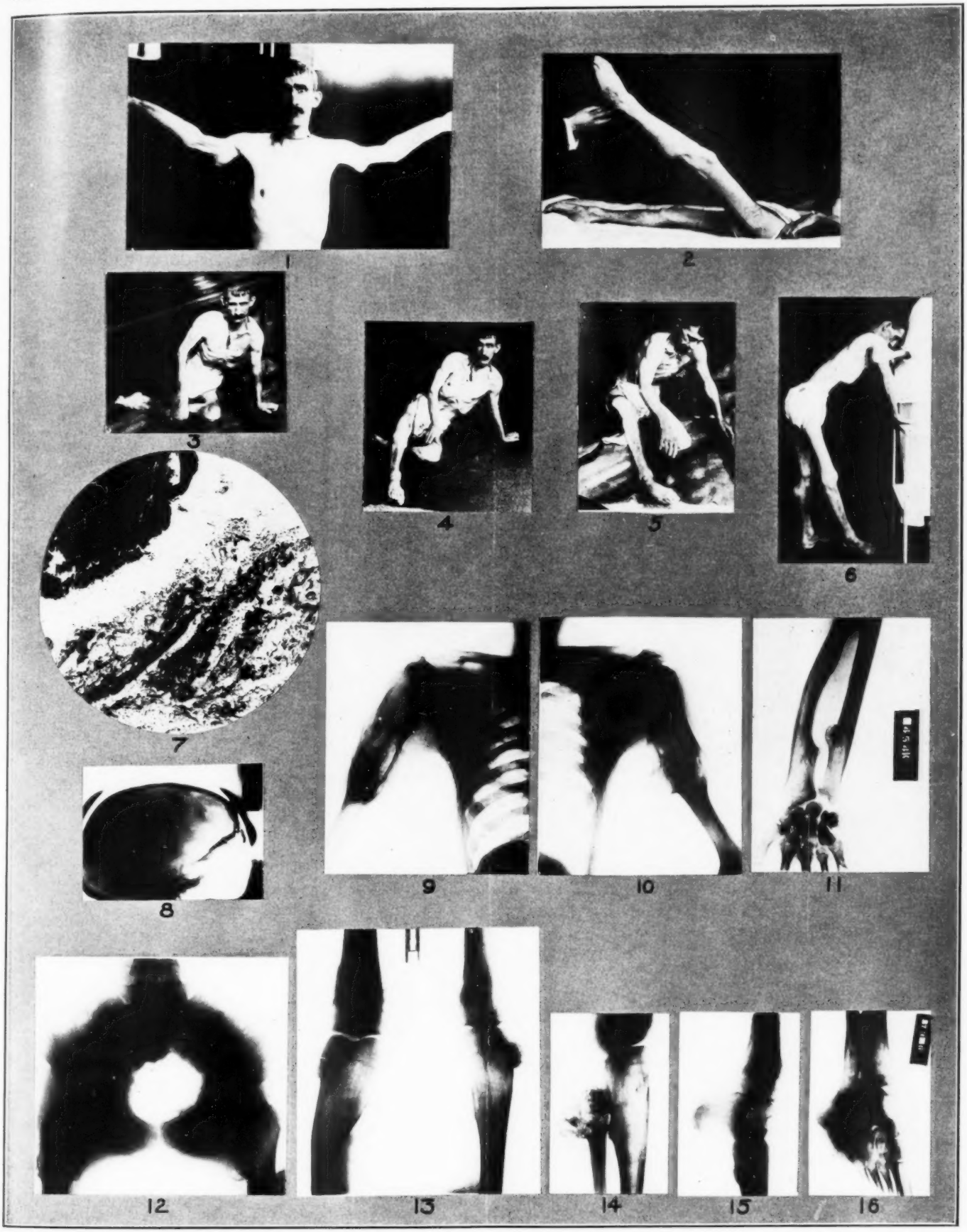
***Family History.*—Father, who was killed in an accident, had "bony lumps" on both legs. Mother dead, cause unknown to patient. Three sisters and one brother living and well. None have any bone tumors or other congenital defect.**

***Past History.*—The patient does not remember any illness until present illness. Sisters say he was born with lumps on legs and arms and, while never very active, was healthy and able to work. At the time they last saw him, two years before admission, he was apparently well and not deaf.**

He denies any venereal infection. Has always been thin and had worked as teamster until about eight months before admission, when his legs became too weak.

***Present Illness.*—Legs have been weak for some time; he had to give up work about six or eight months ago. Did not feel sick. He does not know when deafness came on, but not more than a year or so ago. No pain or discharge from ears preceded or accompanied it. Says he can see as well as ever and that his legs are no worse.**

***Physical Examination.*—Medium-sized, under-nourished man. Seems fairly bright and intelligent. Absolutely deaf, but can read the lips a little. Reads large print or writing very slowly and not altogether with full comprehension. Voice is low pitched, flat and husky, does not volunteer any remarks. Skin rather dry and rough, faint diffuse, brownish pigmentation.**



1-2-3. Photographs showing distribution of tumors.
4-5-6. Attitudes in rising from floor (dystrophic climbing).
7. Section of excised muscle showing atrophy.
8. Skull. Normal sella turcica.
9-16. Radiograms of skeleton.
11. Characteristic bowing of overgrown radius.
12. Large mass in the pelvic strait.
14. Tumor on left fibula showing cystic changes.

Eyes: Deep set. Scleræ visible all around iris, giving a peculiar stare. Slight von Graefe. Winking normal. Movements of eyeballs and lids normal. Pupils equal, react to light and accommodation. Fundi show clear-cut, pale discs with pallor more marked to temporal side. Veins and arteries small. No exudate or hemorrhages. Double optic atrophy of moderate grade. Visual fields show extreme general contraction to a small area about each fovea.

Ears: Apparently deaf for air conduction. Cannot satisfactorily test for bone conduction, as patient does not understand what is wanted. No spontaneous nystagmus. After irrigation with cold water there is normal nystagmus response on both sides, showing that both vestibular nerves are intact. External ears and tympani apparently normal.

Nose, pharynx, tonsils, and larynx normal. No general or local glandular enlargement.

Thyroid: The neck is thin and the tracheal rings easily felt from the cricoid down below episternal notch, but no thyroid isthmus is palpable; lateral lobes cannot be made out.

Lungs: Slight impairment to percussion at both apices, generally enfeebled breath sounds, but no râles of any kind.

Heart: Normal in size and rhythm, no murmurs. Pulse good volume, regular, 70 to minute. No marked sclerosis. Systolic blood pressure 100 mm. (Tycos).

Abdomen: Rather scaphoid; no enlargement of liver or spleen. Colon seems rather full of pasty feces; large bony mass in left iliac fossa.

Genitalia: Normal. Hair normally developed over body.

The patient stands with legs wide apart, and walks with a steppage gait. When placed prone on the floor he gets up with difficulty, climbing up his legs like a dystrophic child. (See photographs.)

Musculature: Facial muscles and tongue normal. Considerable atrophy of shoulder girdle groups, and intrinsic muscles of hands. All the normal movements preserved. No fibrillation. Muscles of trunk seem small but normally active. Wasting of thigh and leg muscles on both sides, more marked on left. Extreme talipes equinus. There is marked weakness, but no paralysis. The peroneal and anterior tibial groups very much wasted. No fibrillation.

Electric Examination: Marked decrease in electric excitability without *qualitative* changes; *i. e.*, no reaction of degeneration. Suggests condition similar to dystrophy, or progressive muscular atrophy.

Sections of left tibialis anticus show marked atrophy with some hypertrophic fibres and supernucleation.

Nervous System, General: Deep reflexes slightly exaggerated. Plantar response (Babinski) normal. No clonus. No sensory changes. No ataxia. No spasticity.

Bones: Skull small, but normally proportioned. Mandible normal. No exostosis made out.

Spine: No abnormalities made out, except that apparently there are six lumbar vertebræ and one less in sacrum.

Pelvis: Thickening of os pubis, huge exostosis projecting from left under side of ilium. Clavicles thickened at inner ends. Scapulæ and ribs normal to palpation.

Arms: Upper third of both humeri much thickened and irregular. Hand normal. Large, irregular exostoses, size of a man's fist, project from inner aspect at junction of upper and middle third. These are very hard, with small flaccid bursæ at outermost points of each, containing a few bean-sized bony, or calcarious, bodies. The lower ends of humeri seem normal. Exostoses on both ends of the forearm bones. Radii overgrown and bowed outward. Small spur on each first metacarpal. Some irregularity at bases of first phalanges. Other bones of wrists and hands normal.

Legs: Upper ends of thighs much thickened, several spine-like outgrowths on each shaft. The fibulæ show very large, bony tumors at the head, the left larger. These are irregular, firm, and no bursæ are felt. The bony masses, as large as an orange, contrast strangely with the atrophic legs. Exostoses are present about the malleoli on both sides. Marked talipes equinus, bilateral, but no large exostoses are felt on bones of the feet.

Urine: Faint trace of albumin and a few hyaline casts. No Bence-Jones protein.

Blood: R. B. C. 6,400,000; Hb. 90 per cent; W. B. C. 8,300. Differential count shows normal formula. No anisocytosis. No abnormal constituents.

Wassermann reaction negative.

Spinal Fluid: Pressure 160 mm. (spinal fluid). Slightly yellow, 17 cells per cu. mm. of small mononuclear type. Noguchi butyric acid test positive. Wassermann reaction negative.

Stools: No abnormal constituents.

X-ray Examination: Rarafaction of bones, with numerous exostoses of osteochondromatous type, symmetrically disposed on extremities and on pelvic bones. The largest tumor at the head of left fibula, is apparently cystic. The skull seems entirely free from exostoses and the sella turcica is normal in size.

Summary: Young man with multiple congenital osteochondromata (father similarly affected).

Thyroid Atrophy. Later, development of degeneration in acoustic and optic nerves; and muscular dystrophy.

No similar cases have been found in searching the literature. The case probably represents congenital defects in the nervous system, as well as in the bones. The X-ray photograph of the skull shows a normal sella turcica, and the escape of the vestibular nerves on both sides, while the acoustic nerves are completely degenerated, make it certain that the nerve changes cannot be due to pressure from exostoses. Whether the thyroid atrophy has any bearing on the bony or nervous changes cannot be more than suggested.

Special thanks are due to Dr. H. M. Thomas for his interest in the neurological examinations, to Dr. S. J. Crowe for his notes on the ears, nose, and larynx, and to Drs. F. H. Baetjer and Charles Waters for the numerous skiagrams.

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THE PATHOLOGY OF SYPHILITIC AORTITIS WITH A CONTRIBUTION TO THE FORMATION OF ANEURYSMS.

By M. C. Winternitz, M. D.

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With Three Figures.

The characteristics of syphilitic disease of the aorta, are now well recognized. Among the still unsettled questions in this relation is the formation of aneurysms. While it is contended by a few that aneurysms form in the stage of acute gummatous degeneration, the general opinion is that they form later, after the medial fibrosis has taken place. The recent occurrence of an early lesion of syphilis of the aorta with minute aneurysms lends positive evidence to the first view.

The following notes will review in brief sequence the historical and pathological development of the subject of syphilis of the aorta; the differentiation of ordinary arteriosclerosis from syphilitic aortitis; the specific nature of syphilitic aortitis; its occurrence as a congenital lesion and, finally, the relation of the lesion to the formation of aneurysms.

Historical.—Until recently the conception was general that syphilis only affected the aorta inasmuch as it was an important etiological factor for the usual arteriosclerotic process, *i. e.* endarteritis chronica deformans, nodosa or atheroma. Especially from the clinical side was this emphasized. The early age at which aneurysms often occurred, a decade or more before the age of arteriosclerosis, led to the belief that syphilis brought about a markedly severe and early sclerosis. The association of syphilis with aneurysms was emphasized by Welch [1] on account of the numerous aneurysms which occurred in young people in the English army. Antisyphilitic treatment was without beneficial results upon aneurysms (Fournier) except in a few isolated cases (Verdie see Benda). Statistically varying numbers of aneurysms from 95 per cent (Heller [2]) to 18.75 per cent (v. Hansemann [3]), were found associated with syphilis.

Such authors as Virchow [4] and Welch [l.c.] even though they realized that there was an intimate association between syphilis and aneurysm production only believed that syphilis brought about an early and marked sclerosis of the usual type, from which the aneurysms developed secondarily. On the other hand, definite active or even gummatous lesions of the aorta have been described both with and without aneurysms, as for instance, the case of Wilks [5] in 1863 associated with aneurysm, and that of Wagner [6] unassociated with aneurysms.

The first description of the specific appearances particularly the macroscopic appearances of syphilitic aortitis, dates back to 1866 (Wagner [6]) and 1873 (Hemlstedter [7]). These authors recognized that the process was different from the usual atheromatous changes, but they did not realize its specific nature, and Helmstedter though describing the microscopic lesions of the media considered that they were the result of mechanical rupture of the elastic lamella with replacement fibrosis. Hertz [8] likewise described the macroscopic lesions in 1873 and Vallin [9] in 1879, but they considered the lesion a simple form of arteriosclerosis. Heiberg [10] in 1876 not only described the macroscopic but also the microscopic changes. He recognized the latter and considered them as analogous to the changes described by Köster, *i. e.* a cellular infiltration in the media and about the vasa vasorum and partial obliteration of the vasa vasorum. Heiberg considered that the localized zones of cellular infiltrations might be recognized as miliary gummata. Soon after this Laveran [12] described a similar case and independently noted the presence of miliary gummata in the media. In 1880 Snow [13] recognized an important characteristic of the specific aortic lesion, *i. e.* obliteration of the mouth of one of the large vessels in a case of aortic aneurysm in a young syphilitic girl. Köster [14] in the same year gave a detailed description of the specific lesion. He called it a mesaortitis and considered syphilis as the etiological factor. He did not regard the change as a specific syphilitic process, inasmuch as he did not think that it differed from the usual arteriosclerotic process except in intensity and extent of involvement.

Despite the above and other valuable preliminary reports, the real significance of the specific syphilitic lesions of the aorta and their importance in the etiology of aneurysms was only realized after the numerous contributions by the Kiel school. These writers opposed, and after many years overthrew the theory that syphilis was one of the factors in the production of the ordinary forms of arteriosclerosis, and established the gross and microscopic lesions which to-day are recognized in the vast majority of instances at least to be the result of a typical gummatous syphilitic lesion and quite distinct from other forms of arteriosclerosis.

Döhle's [15] first communication (1885) was the beginning of a series appearing from the Kiel laboratory. He described the lesions occurring in a 25-year-old man with outspoken lues of various organs. The aorta, particularly in the ascending and to a lesser extent in the descending thoracic portion showed larger and smaller ballooonings of its wall. There were only a few yellowish elevations in an otherwise normal intima. Microscopically there was a diffuse infiltration of round cells in the media; in places masses of round cells and blood vessels occupied clefts in the media; here and there bands of fibrous connective tissue were found running through the media and joining the adventitial and intimal coats, retracting the latter which otherwise was very little changed. The adventitia showed inflammatory changes similar to those described in the media, although somewhat less pronounced. Döhle concluded that the cellular infiltrations in the media were gummata which subsequently became converted to scar

tissue and that the entire process except the intimal thickening which he regarded as a diffuse proliferating endarteritis was peculiar to syphilis. Döhle's [16] second report in 1895 included two similar cases. He concluded from their study that the lesion was recognizable macroscopically by radiating scarred depressions and indentations of the intima, and that these were caused by luetic lesions of the media and adventitia.

A series of papers by Backhaus,[17] Philips,[18] Moll,[19] Isenberg [20] and Heller [21] supported Döhle's view. Heller sums up the situation in 1903 as follows: Macroscopically there are always scar-like depressions and furrows on the inner side of a conspicuous syphilitic aortitis. Microscopically, above all there is a cellular infiltration in the media, and it is not rare to find multinucleated giant cells and necrotic areas in these proliferations which may be called miliary gummata. Occasionally large caseous areas occur. From the cellular proliferations fibrous scars arise. Secondarily, the intima may be thickened but this thickening has no tendency to undergo atheromatous degeneration, and has, on the contrary, a stiff scar-like contracted character. The adventitia is variably affected. It may be sclerotic and the vasa vasorum may be entirely occluded. Heller says the diaghosis of the specific lesion is often made difficult, on account of the frequent combination of a syphilitic with an ordinary atherosclerotic process.

This view of syphilitic disease of the aorta as conceived by Heller and his school was accepted by a large number of writers (Buchwald, Jacob, Crooke, Belfanti, Abramow, Heiberg, Puppe, Rasch, Straub, Benenuti and others cited by Chiari [22]). Rasch [23] pointed out that the intimal thickenings were not yellow, but a dull gray and that the lesion was confined most often to the thoracic aorta. Straub [24] added that the process was often most intense at the origin of the larger branches, as in the arch and that the process was often confined to the thoracic aorta, sometimes extending to the upper portion of the abdominal aorta. Further the lower edge of the process often ended abruptly and had a sharp line of demarcation.

The Differentiation of Arteriosclerosis From Syphilitic Aortitis.

The following description and differentiation of the usual form of endarteritis chronica deformans (arteriosclerosis) of the aorta and aortitis of syphilitic origin may be abstracted from Chiari's masterful description.

Arteriosclerosis begins in the intima with swelling of the tissue, increase in local cells and fatty degeneration of these. Often it seems as though the fatty change may have been primary. Following these changes there is an increase in the connective tissue of the intima which has a tendency to undergo a hyaline, fatty or mucoid degeneration, necrosis or calcification. Frequently there is a new formation of elastic tissue. At first the media and adventitia are normal, but later these layers also become involved. The inner layer of the media undergoes a degeneration similar to that in the intima and in its outer layers there may be a moderate proliferation of blood vessels together with a mild grade of cellular and connective tissue proliferation. In the adventitia there may be a round cell infiltration along the course of the vasa vasorum and the latter may show an endarteritis proliferans. The inflammatory changes of the intima and media, however, are confined within narrow limits and Chiari says, he has never seen any degree of mesaortitis or periaortitis in pure endarteritis chronica deformans. Under specific conditions proliferation in the media may occur in localized areas, for instance, below a large, fatty or calcified plaque in the depths of the intima, and pressing on the media. In such instances there is a proliferation of connective tissue through the media towards the plaque which acts like a foreign body. Chiari could not confirm Köster's idea that the intimal thickenings are always secondary and the result of a mesaortitis arising from the vasa vasorum, nor could he agree with Martin that there is always an endarteritis proliferans of the nutrient vessels resulting in a fatty degeneration and inflammatory proliferation of the intima. He agrees, however, with Virchow that there is a "parenchymatous proliferation" in the intima without there being any appreciable involvement of the blood vessels. He also agrees with Marchand that the early changes in arteriosclerosis are associated with a nutritional disturbance of the vessel wall which manifests itself in a swelling, thickening and sclerosis of the intimal tissue, an increase and subsequent degeneration of the cellular elements frequently followed by partial necrosis and calcification. In other instances the most conspicuous change is an indurative thickening of the intima. Both the degenerative and inflammatory involvement of the media and adventitia are secondary. They are in part a reaction against the degeneration, and in part play the rôle of a reparative process. The etiological factors for this type of aortic change are numerous and are associated with intimal or medial damage caused by mechanical, infectious, and other agents.

The above series of changes are in marked contrast with those that occur in syphilis. Here the affection of the adventitia and media plays the title rôle, and appears to be primary while the intimal thickening only develops secondarily. Chiari says that microscopically syphilitic aortitis is similar to the above described arteriosclerotic process with the following peculiarities: There is less tendency for the intimal proliferation to undergo regressive metamorphosis. The intimal changes in comparison to those of the adventitia and media are often strikingly slight or in the early stages of the disease entirely lacking. The lesion is further identified by the frequent occurrence of furrows and wrinkles on the inner side of the aorta and finally by its regular occurrence in the ascending portion of the aorta, descending on the one hand to the semilunar valves and on the other across the arch and the descending aorta rarely as far as its abdominal portion. The diseased process frequently stops abruptly above the abdominal aorta.

Microscopically the medial changes are the most striking. They consist of inflammatory areas which appear partly as accumulations of round cells, partly as vascular granulation

tissue. These zones extend from the adventitia through the media, towards the intima and run at right or oblique angles to the axis of the vessel. Giant cells similar to the Langhans cells found in tuberculosis may be present in the inflammatory zone. The granulation tissue surrounding pieces of necrotic media may also contain giant cells, partaking more of the nature of foreign body giant cells. The fibrous connective tissue arising from these areas of necrosis tends to contract and in this way produces the depressions and wrinkles of the surface. The adventitia shows an inflammatory reaction. The younger areas appear as masses of round cells and granulation tissue situated along the vasa vasorum while the older manifest themselves as dense fibrous connective tissue. The vasa vasorum show an endarteritis proliferans. The intima presents a variable picture. It may be unchanged, moderately or greatly thickened. The latter has little tendency to undergo regressive metamorphosis; on the other hand it may present an ordinary endarteritis chronica deformans, *i. e.*, thickenings with marked fatty degeneration and calcification.

Chiari believes that this second type of aortic disease is a distinct anatomical form, and should be separated from the usual types of chronic deforming endaortitis. He concludes from his studies that absolute scientific security in the diagnosis as luetic of such a productive mesaortitis will only be arrived at when we have more complete knowledge of the virus of syphilis. Further that he would not desire to exclude the possibility that a similar anatomical picture may be brought about by a different etiological agent. Still he considers that the findings of a productive mesaortitis should be regarded primarily as a syphilitic process.

Many were skeptical concerning the specificity of syphilitic mesaortitis. Heine [25] comments that he does not consider every mesaortitis as syphilitic, and that after the scars have formed he thinks there is no longer any criteria concerning their etiology. Ribbert [26] also did not consider the proof sufficient and Marchand [27] says that while it is true that many aneurysms occur in syphilitics, attempts to demonstrate changes in the blood vessel wall of a specific luetic nature are not always attended with good results, as they may not be present in the later stages. He believes that similar lesions may occur without lues, but grants that probably most of them are luetic.

With the discovery of the spirochæta pallida as the etiological agent for syphilis a more direct means has been put at our disposal for the determination of the specific cause of this disease of the aorta. Unforunately here as in the other tertiary lesions of the disease difficulty has been experienced in demonstrating the organisms. In favorable instances and in earlier lesions they are present in large numbers in the areas of round cell infiltration and necrosis of the adventitia and media, and have been demonstrated in such instances by Reuter,[28] Schmorl,[29] Benda,[30] Wright and Richardson [31] (5 cases), Wright [32] (3 cases) and Klotz.[33]

On the other hand the Wassermann reaction has been of great aid in demonstrating the specific luetic nature of mesaortitis. To quote from Pearce,[34] for instance, the combined statistics of Noguchi, Swift, Bruch, Kaplan, etc., show that the reaction was positive in from 63 to 89.9 per cent of 1878 cases of tertiary syphilis while it was only positive in from 0.3 to 1.1 per cent of 5,946 non-syphilitic cases. With this as a basis Pearce has collected the results of the Wassermann reaction in a large number of cardio-vascular cases and finds that it is positive in 66.6 per cent of aneurysms 69.6 per cent of aortic insufficiencies 23.5 per cent of other valvular lesions, and in 81.45 per cent of cases of mesaortitis. From these results Pearce correctly concludes "that the general theory concerning the association of mesaortitis, aortic insufficiency and aneurysm, and the relation of these conditions to syphilis is supported."

One of the more interesting recent findings and one which at least lends absolute evidence to the above idea that mesaortitis is frequently caused by syphilis, if even further reaching conclusions may not be drawn, is the fact that a similar lesion of the aorta has been described in congenital syphilis. This lesion has become established through the work of Hasselbach, Wiesner,[35] Rach and Wiesner,[37] Klotz,[33] etc. The congenital lesion seems quite analogous to the disease in the adult.

It appears from the studies of the congenital lesions that every syphilitic aortitis is not necessarily a mesaortitis since in several cases of fresh congenital syphilitic aortitis huge numbers of spirochætæ were demonstrable in all the tissues of the aorta, particularly in the intima. The various coats of the aorta were affected by the presence of the organism and had reacted to its irritation. Mesaortitis may be the most common picture of syphilis of the aorta, still it is not the only type and therefore mesaortitis and syphilis of the aorta may not be considered as synonymous.

The demonstration of the spirochæta pallida in the aorta in congenital lues is of interest. Rach and Wiesner examined 27 cases of congenital lues; 16 per cent of these showed typical lesion of the aorta, but in only four were the organisms demonstrable. The organisms were so situated that no relation between the local lesions and the position of the organisms could be established.

The Relation of the Diseased Process in the Aorta to the Formation of Aneurysm.

Helmstedter l.c. and Mahchot [39] considered the basis for their questionable disease of the aorta to be a primary rupture of the elastica, while Köster, and others believed that it was the result of an inflammatory process in the media. Heller considered it a specific luetic condition. All of these authors agreed that the formation of aneurysms was associated with the replacement of these areas of injury in the elastica of the media by fibrous tissue. They considered that the scars offered less resistance to the pressure within the vessel, and consequently allowed aneurysms to form in these areas. This was the accepted view to which Benda has taken exception. He says that the conception that the elastica is responsible for the distensibility of the arteries particularly the aorta and that the replacement of the elastica by connective tissue increases the distensibility in these areas is not in harmony with other physiological and pathological experiences. The

leimgebende Bindegewebs-fibrille are practically non-elastic, as we encounter them in tendons and scars. He continues that while the media is elastic it is easily broken, but that the adventitia is neither elastic nor easily broken. The apparent elasticity of the adventitia is due to the fact that the connective tissue fibres when at rest are wrinkled. The toughness of the connective tissue of the adventitia is demonstrated in dissecting aneurysms where, having ruptured the media, the blood is held in by the adventitia. The resistance of the adventitial connective tissue hinders the overdistention of the elastica. A rupture of the elastic lamellæ is only possible when there is a preceding or concomitant destruction of the connective tissue fibers. Benda, therefore, concludes that the direct cause of every aneurysm lies in the inflammatory or traumatic destruction of the connective tissue either associated

FIG. 1.

with or followed by the traumatic or dystrophic destruction of the elastica. He further states that if the above statements are accepted the medial scars in mesaortitis are not to be considered in the formation of aneurysms. He admits, however, that their rigidity may bring about harmful results, inasmuch as their lack of elasticity may render them more likely to be the seat of traumatic aneurysm, though to a much less extent than the rigid calcified plaques occurring in endarteritis chronica deformans. Benda [l.c.] believes with Etienne, Hertz, Babes, Puppe and others that the gummatous processes found in the arterial wall are the points of origin of the aneurysm. He agrees entirely with Fabris who came to the conclusion that aneurysms may develop in syphilitic aortitis, as soon as the granuloma has succeeded in destroying a sufficient portion of the arterial wall. These specific granulomata Fabris believes begin in the periadventitial connective tissue and in the adventitia from whence they gradually involve the media and terminate with necrosis of the media and intima. In all probability the saccular dilatations occur at this time.

The following case confirms this view of Fabris and Benda.

Colored female, age 29 years. Autopsy No. 3565.

Clinical History.—The patient was a maid in the service of one of the attending physicians of this clinic. As far as could be ascertained she had been well until the present illness, with the exception of a fever, supposed to be malarial, during the summer of the past year. About two weeks before death she began to have headaches, but seemed well otherwise. She worked the entire day and was found dead in bed the following morning.

Anatomical diagnosis: Syphilitic aortitis with multiple small aneurysms one of which pressed upon and occluded the posterior coronary artery; coronary thrombosis below aneurysm; chronic pelvic peritonitis.

Heart.—The heart is normal in size and external appearance.

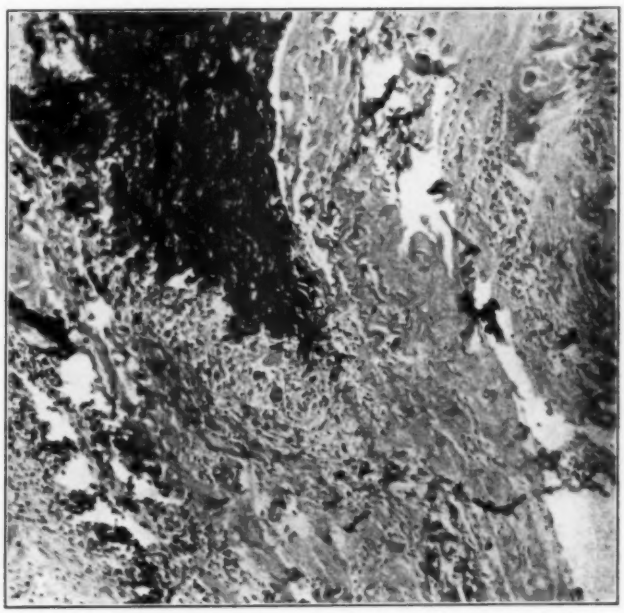

FIG. 2.

Its cavities and valves as well as the myocardium are unaffected. The base of the aorta shows a few small yellowish plaques, one of the larger ones being situated just at the mouth of the anterior coronary artery. Just above and to the left of the mouth of the posterior coronary artery there is a pouching of the aortic wall about 0.5 cm. in diameter. Projecting from the mouth of the posterior coronary artery is a recent small friable clot of a grayish yellow color. It is not adherent to the vessel wall and extends into the coronary artery for a distance of 1 cm. where the vessel is found to be in contact with the apex of the small aneurysmal sac above described. Around the mouth of the above sac the intima of the aorta is thickened, grayish in color and broken. On cutting through, the wall of the aorta may be seen to be thickened. This thickening is most marked in the adventitia, which is grayish in color and contains numerous small capillaries, distinguished by their bright red color. Several similar aneurysms though smaller may be seen at the origin of the aorta. Otherwise the vessel appears normal and quite elastic. The other organs show nothing of particular importance.

The microscopic findings are illustrated in the three accompanying figures. Figure 1 is a photomicrograph of the aneurysmal

sac. In the region of the sac the intima may be seen to be slightly thickened, but shows no tendency to undergo retrogressive metamorphosis. The sac is best outlined by the media which is particularly conspicuous since the elastic tissue has been specifically stained. The media may be seen to be quite irregular and at the apex of the aneurysmal sac it is considerably fragmented and invaded and replaced by a cellular granulation tissue. The adventitia is very markedly thickened. Figure 2, a higher magnification of the apex of the aneurysmal sac, shows the broken elastic tissue lamellæ surrounded by a granulation tissue. At the very apex of the pyramid formed by the elastic tissue fibers a miliary gumma composed of giant and epitheloid cells is found replacing the adventitia. Throughout the remaining portion of the adventitia there is a similar cellular infiltration. The third picture is simply a higher magnification of the miliary gumma at the apex of the pyramid formed by the broken media.

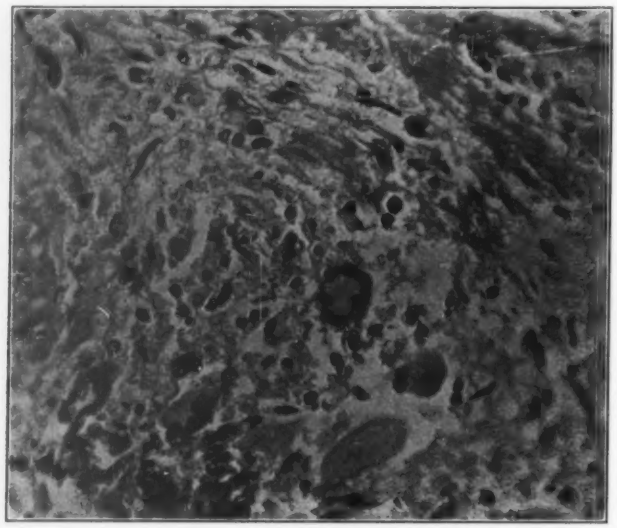

FIG. 3.

CONCLUSIONS.

There is no evidence in favor of the view that the medial fibrosis occurring in aortitis is the source of the aneurysms occurring in this condition.

On the other hand the case report included in the above article shows an aneurysm in its incipiency with the minute sac extending through the acutely broken and necrotic media to the adventitia where there is a specific granuloma present. This indicates that aneurysms of the aorta may form in the active stage of syphilis.

The adventitia shows the specific granulomatous process most characteristically. An extension of the inflammation from the adventitia to the media no doubt plays an important rôle in the destruction of the medial fibres. In addition the rupture of the elastic lamellæ may depend in part upon the diminished support offered by the non-diseased adventitia.

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AORTIC ANEURYSM RUPTURING INTO THE PULMONARY ARTERY, WITH A REPORT OF THREE CASES.

By HOLLAND NEWTON STEVENSON, M. D.

(From the Pathological Laboratory of The Johns Hopkins University.)

Aneurysms rupturing into the pulmonary artery are infrequent as is shown by the occurrence of only three in the post mortem records of The Johns Hopkins Hospital. One of these was encountered in a recent case, the other two were obtained from the autopsy records. In two of the cases the aneurysmal sac was large and had a free opening into the pulmonary artery. It is interesting to compare the physical signs of these two cases with those of the third case, which had a small sac and a recent pin-point perforation into the pulmonary artery.

Cases of thoracic aneurysm rupturing into blood vessels are not particularly infrequent, the usual sites being the inferior vena cava, the superior vena cava or the pulmonary artery. Osler states that those rupturing into the pulmonary artery are probably most frequent; those rupturing into the superior vena cava next in frequency; and those rupturing into the inferior vena cava least frequent. Among the 3900 autopsies at The Johns Hopkins Hospital, the three cases below reported are the only ones of perforation of a thoracic aneurysm into the pulmonary artery. In 1907 Kappis collected 32 cases from the literature of aortic aneurysm perforating into the pulmonary artery and reported a similar case. Three of these cases were complicated by rupture into the ventricle. He refers to other similar cases, reported without autopsy findings. The clinical features and physical signs of the cases presented are discussed at length. Since Kappis' publication, reports of individual cases of the same type have been made by Hollis in this country and by Lenoble and Chapel in France.

CLINICAL HISTORY—CASE I.—I. B., colored male, admitted to the service of Dr. L. F. Barker of The Johns Hopkins Hospital, September 19, 1912, complaining of shortness of breath. His family history is unimportant as is also his personal history, except that he has had several attacks of gonorrhœa; he gives no history of syphilis. His present illness started about Christmas, 1911, with sudden shortness of breath which has continued and become aggravated. Associated with this there was precordial pain, swelling of the legs, abdomen, and extremities. During the latter part of his illness there have been severe coughing spells associated with considerable blood-stained sputum and nausea.

Physical Examination.—The patient is a well nourished colored man, sitting up in bed, resting on his arms. He has marked dyspnœa and is apparently in great pain. The physical signs may be briefly summarized as follows: The veins of the neck are greatly dilated, and there is a whirling murmur over the subclavian arteries. There is no definite tracheal tug but a definite transmitted pulsation may be felt over the trachea.

Thorax.—The percussion note is impaired and almost flat over the right base and above the spine of the scapula on the left side with suppression of the breath sounds in these areas. There are numerous moist râles at both bases.

Heart.—The point of maximum impulse is not very definitely localized in the fifth interspace in the mammary line. There is a diffuse heave to the whole sternum. In the third interspace just above the nipple and along the left border of the heart there is a localized pulsation where a friction fremitus, synchronous with the heart beat, is felt. The relative cardiac dullness begins at the second rib and extends 14½ cm. to the left in the 5th interspace, and 5½ cm. to the right in the 4th interspace. On auscultation at the apex a systolic blow accompanies the first sound which is loudest and most intense near the sternum. At the base and just to the left of the sternal border a diastolic murmur is heard. The pulmonary second sound is accentuated. In the area where the fremitus is palpable, on auscultation there is a machinery-like whirl, made up of a rough systolic murmur, an accentuated second sound and a blowing sound that runs through both diastole and systole. The pulse in the two radials is equal but definitely collapsing. There is a shifting dullness in the flanks. The extremities are markedly œdematous, the tissue pitting with difficulty.

Death occurred rather suddenly on the second day after admission. The patient called for a sputum cup, expectorated a small amount of blood-streaked sputum, which was followed by pure blood. This gushed from his nose and mouth and ended in collapse and death within a few minutes (1100 cc. being collected).

Autopsy, No. 3779, was performed two hours after death.

Anatomical diagnosis.—Syphilitic mesaortitis; aneurysm of the transverse arch of the aorta communicating with the pulmonary artery; marked hypertrophy of the right ventricle; chronic passive congestion of the viscera; ascites; terminal rupture of aneurysm into left lower bronchus.

Body is that of a rather well nourished colored male. There is œdema of the extremities and body wall. The abdominal cavity contains about 250 cc. of a clear fluid. The right pleural cavity contains 2 litres of blood-stained fluid and a few fibrous adhesions are present. The left pleura contains about 500 cc. of a similar fluid and numerous old fibrous adhesions. The pericardial sac has an excess of straw-colored fluid.

The *heart* is greatly enlarged and weighs 740 gms. with aorta and aneurysm. The right auricle is dilated and its wall is slightly hypertrophied. The tricuspid ring measures 14 cm., the valves being delicate. The right ventricle is greatly hypertrophied. The columnæ carneæ stand out prominently and the wall measures 9 mm. The pulmonary ring measures 9¼ cm. The valves are delicate. The vessel wall shows nothing abnormal. The left auricle shows no definite changes. The mitral ring measures 11 cm. and the valves are everywhere delicate. The wall of the left ventricle is 16 mm. thick. The aortic ring measures 9 cm. The aortic valves show no change. The surface of the aorta is everywhere smooth and glistening except for a few, scattered, small, yellowish, opaque spots and streaks. The myocardium is apparently normal as are also the coronary vessels.

Aneurysm.—Opposite the orifice of the carotid artery and 8 cm. from the aortic ring, there is a large opening in the wall of the aorta 9 cm. in circumference which communicates with an aneurysmal sac. This sac arises from the anterior and in part from the inferior wall of the transverse arch of the aorta and extends inferiorly to the pulmonary artery which it overlaps; and anteriolaterally to the left, where it is adherent to the upper lobe of the lung. There are two communications between the sac and the pulmonary artery where they are in contact. The larger is round, and 1 cm. in diameter. It is on the anterior surface of the pulmonary artery 5¼ cm. from the pulmonary ring. The smaller is oval 2 mm. by 1 mm. in size and is about 7 mm. above the larger communication.

These orifices have well rounded and smooth edges. The lateral wall of the sac shows two more openings where it is adherent to the lung. The one about 1 cm. in diameter, opening into the primary bronchus to the lower lobe; the other, much smaller, opening into a secondary bronchus. The lining of the aneurysmal sac is rather corrugated and covered with a thin layer of fibrin.

Lungs.—The left upper lobe is collapsed and non-air containing. The lower lobe is dark purple in color and on section it is firm and of a homogeneous dark purple color. On opening the trachea it is filled with a recent clot.

The other organs show nothing of specific interest, being only typical examples of chronic passive congestion.

Clinical History—Case II.—J. S., white male, age 26, admitted to the clinic of Dr. L. F. Barker on January 10, 1910, complaining of pulsation of the heart. His family history is negative.

Personal History.—He has always been well. He has had no venereal disease, but admits frequent exposure. On December 4,

Aneurysm of Case I.

1908 he was admitted to the hospital when the following clinical note was made: "Patient is well nourished but pale. The carotid pulsations are marked. The pulse is larger on the right than left and is a well marked, water-hammer pulse. There is distinct precordial fullness above and inside of nipple, which is most marked in the second interspace 5 cm. from the mid-sternal line. Retraction in the 4th and 5th interspaces. There is a visible and palpable rebound over the pulsating area. The lungs are negative on auscultation and percussion.

"*Heart.*—The point of maximum impulse is not definitely localized. The relative cardiac dullness extends to the left; 15 cm. in the 5th interspace; 13½ cm. in the 4th interspace; 14½ cm. in the 3d; and 14 cm. in the 2d. To the right it extends 4½ cm. in the 3d interspace. At the apex, and best in the 4th interspace just inside of the dullness, the first sound is sharp and followed by a short, snappy blow well heard in the back. In the axilla and back the first sound has a tapping character suggesting mitral stenosis. The second sound is barely audible at the border of dullness, but as one approaches the mammillary line in the 4th interspace a distinct ringing second sound with a peculiar echoing quality is heard. In the 3d interspace there is a continuous machinery murmur with systolic accentuation. A very slight second sound is audible.

"In the 2d left interspace, in the midst of the general echo a distinct to and fro diastolic murmur is audible and a well marked second sound close to the sternum. In the aortic area a diastolic murmur is heard along the left border of the sternum. The to and fro murmur is heard associated with the second pulmonic. To the right of the sternum a blowing systolic murmur with a sighing quality is well audible. The second sound is rather sharp. The heart is fixed in position."

On December 18, 1908, the *aneurysm was wired* by Dr. J. M. T. Finney, following which the patient's condition became improved and he was discharged in June, 1909. In November of the same year he caught cold and suffered much pain in his chest on coughing.

Four weeks before his final admission he became puffy under the eyes. He had many vomiting spells and much shortness of breath. When admitted, January 10, 1910, the following clinical note was made:

The patient is sitting up in bed by preference, resting on his arms. He shows some loss of weight, his lips and ears are cyanotic, and the mucous membranes are pale. The vessels of the neck are full, being more so on the right. In the carotids there is a systolic thrill and on auscultation a continuous hum with systolic accentuation is heard. The pulse is collapsing, that on the left being smaller than the right. A definite tracheal tug is felt. There is a diffuse heave of the chest with systole and there is a marked pulsating prominence above the left precordium. The lungs are clear, except for impairment at both bases.

Heart.—The point of maximum impulse is 14½ cm. to the left in the 5th interspace and rather indefinite. There is slight systolic retraction of the lower part of the thorax. The expansile impulse is localized in the 1st, 2d, 3d and 4th interspaces where a continuous thrill with systolic accentuation is felt. The relative cardiac dullness is continuous with the pulsating mass and extends to the left; 16 cm. in the 5th interspace, 12½ cm. in the 3d, 11½ in the 2d, and 10½ in the 1st interspace. It extends 5 cm. to the right in the 4th interspace. At the apex, the sounds are feeble and a very loud systolic murmur is heard, which is well transmitted, and an equally rough diastolic murmur. These are maximal along the left border of the sternum. At the base the second pulmonic is loud, snappy, and accentuated. Over the pulsating area a continuous rough murmur is heard having a systolic accentuation. Both sounds are heard here but the second sound is very loud, snappy and accentuated. These sounds and murmurs are heard all over the right front and left back. There is dullness in the flanks and œdema of the extremities.

The patient died on January 11 after numerous coughing and vomiting spells having gradually become weaker.

Autopsy, No. 3323, performed January 11.

Anatomical diagnosis.—Syphilitic aortitis; aneurysm of the ascending arch of the aorta; erosion with opening into the pulmonary artery; compression of vessels and bronchi at the hila; chronic adhesive pericarditis; cardiac dilatation and hypertrophy; chronic passive congestion of the viscera.

Body is that of a well nourished white man with cyanosis and puffing of the face. The liver extends 11 cm. below the costal margin in the mammary line. There is a large amount of fluid in the right pleural cavity. The pericardial sac is obliterated. On the anterior mediastinum is found a mass composed of two portions. The upper is a large spherical mass, 10 cm. in diameter, which gives on palpation the sensation of a thin sac in the wall of which are thin pieces of shell. Beneath this is felt a muscular organ. The former mass is firmly adherent to the parietal wall.

Aorta.—From the bifurcation up to the arch, the aorta shows only a few scattered atheromatous patches. The arch is normal as is its ascending portion along its posterior surface, but on its anterior and left surface, about 6 cm. from the aortic ring, is a great dilatation of the vessel, having a definitely circumscribed mouth, formed by a ridge of elevated yellowish tissue which is of a firm cartilaginous consistency. This opening occupies the concave and anterior portion of the ascending arch, commencing 1 cm. from the aortic valves. The sac extending from this opening is large and contains a recent clot, collected around silver wire. The wall is irregular and corrugated, being covered, especially opposite the orifice, with laminated clot, but being thin in some places and having areas of calcium deposits. The sac presses the pulmonary artery to the left and posteriorly, and the wall of this vessel has become thinned, and there is a hole in it 6 mm. in diameter, 1 cm. above the pulmonary orifice.

Heart.—The right auricle is dilated and its wall thinned where it was in contact with the aneurysm. The tricuspid ring measures 15 cm. in circumference. The valves are delicate and apparently competent. The right ventricle is dilated and its wall thickened, measuring in thickness almost 1 cm. The pulmonary valves are delicate. The left auricle is not extremely dilated and its appendix is fixed in position by adhesions. The mitral ring measures 11½ cm. The valves are delicate. The ventricle on this side shows a thickened wall which averages 8 mm. but is 22 mm. in its thickest part. The aortic valves are slightly thickened and do not seem to be exactly competent. The heart muscle shows only a few translucent streaks of fibrous tissue.

The other organs show chiefly chronic passive congestion.

CLINICAL HISTORY—CASE III.—O. W., colored male, age 45, was admitted to the clinic of Dr. William Osler on January 5, 1892, complaining of shortness of breath and weakness of the legs. From the family history it seems that several members suffered from heart disease. Personal history is negative. Present illness began in October, 1891, with a cold and cough. Four weeks before admission shortness of breath set in with occasional attacks of nausea and vomiting. He could not sleep lying down. His legs and ankles have been swollen only the past few days. There has been some nicturia and some expectoration.

Physical Examination.—Patient is a well nourished man suffering from shortness of breath. He has pale mucous membranes. The pulse is regular but of low tension. The resonance of the chest is good except for flatness at the right base with distant breath sounds in this area.

Heart.—Impulse 2 cm. outside nipple line. Dullness begins at the upper border of the third rib and extends to the right border of the sternum and through the nipple to the apex impulse. No thrill is felt at the apex. On auscultation at the apex the first sound is faint, the second sound is replaced by a dull, prolonged thrill. As one passes upwards a dull murmur becomes more audible, the diastolic being louder and more accentuated on the 3d rib. Three finger's breadth from the sternal margin the second pulmonic is sharply accentuated through the murmur over the base. Approaching the sternum in the 3d interspace the murmurs are heard at their loudest, the diastolic having a somewhat musical character. In the aortic area a double murmur only is heard. A single murmur of moderate intensity is present in the carotid. Abdomen is rather full. There is œdema of the extremities. The patient improved for a short time under rest and treatment, but finally grew weaker and died on January 11, 1892.

Autopsy, No. 267, was performed on January 12.

Anatomical diagnosis.—Aneurysm of aorta; hypertrophy and dilatation of heart; chronic passive congestion of lungs; and abdominal organs; pin-point perforation from aneurysm into pulmonary artery.

Body is that of a large, strongly-built man, with large and turgid veins of the neck. The peritoneum, right pleuræ and pericardium contain an excess of fluid.

Heart weighs 450 gms. The aortic valves appear normal and the aorta is smooth throughout. There is an aneurysmal opening 2½ cm. long near the opening of the left coronary artery, which extends as an aneurysmal sac downwards and backwards along the edge of the valve into the ventricle. The wall of the sac is smooth, but has some pit-like depressions, the deepest of which extends into the sinus of the middle cusp of the pulmonary artery. The projection into the latter is about 2 mm. high; to which prominence the cusp is partly adherent. At the tip of the prominence is a small projection into the pulmonary artery of fresh fibrinous vegetations. At this point is the opening from the aneurysmal sac into the pulmonary artery, which is about 0.5 mm. in diameter. The aortic ring measures 7 cm. The mitral ring measures 11 cm. The myocardium of the left ventricle is 16 mm. thick. The tricuspid ring measures 12 cm. The myocardium of the right ventricle is 6 mm. in thickness. The other organs are typical examples of chronic passive congestion.

Summary.—1. The points of clinical differentiation between the cases with a large communicating opening into the pulmonary artery (Cases 1 and 2) may be contrasted with those of the third case, which presented only a tiny opening, and summarized as follows:

(a) Enlargement of the heart to the right (Cases 1 and 2). No enlargement to the right (Case 3).

(b) A continuous thrill and murmur in the carotid and subclavian (Cases 1 and 2). A single murmur and thrill (Case 3).

(c) In the third left interspace (Case 1) a continuous murmur with an overlying rough, systolic murmur.

Case 2 had a continuous murmur with a systolic accentuation. Case 3 had a systolic and diastolic murmur.

(d) Cases 1 and 2 had a collapsing pulse. Case 3 did not.

2. The origin of the aneurysms was as follows: Case 1, from the transverse arch, in Cases 2 and 3 from the ascending arch of the aorta. The points of perforation into the pulmonary artery were in Cases 1 and 2 on the anterior surface of the artery 5¼ cm. and 1 cm. from the ring respectively. In Case 3 the perforation took place on the posterior wall behind the posterior cusp of the pulmonary valve.

3. That the pulmonary perforation had been present for a relatively long period of time in Cases 1 and 2, is borne out by the immense hypertrophy of the right ventricle, which is not evident in Case 3. The lack of change in the physical signs in Case 2 over a period from 1908 to 1910 also upholds this point.

4. In Case 3 the perforation, although recent, had no bearing on the death of the patient, while in the other two cases it had existed for so long a time that the conclusion can be drawn that perforation of an aneurysm into the pulmonary artery is not incompatible with life.

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ALLERGY AND RE-INFECTION IN TUBERCULOSIS.[1]

By Edward R. Baldwin, M. D., Saranac Lake, N. Y.

It will be noted that my subject as announced in your program presumes to a degree upon the knowledge of newly-coined terms by the audience. Although Prof. v. Pirquet's sojourn here was short, I am sure his admirable studies in the field of hypersensitiveness, or "changed reactions," are well known and appreciated. Since he first applied the word "allergy" to the phenomena of "changed reactions," as a general term, without wishing to convey any theory of its nature, immunology has made further advances. The many manifestations of allergy have been studied exhaustively both in tuberculosis and other diseases, with the result that it is safe to range it under the head of immunity or protective functions. I used the term advisedly in my title to avoid a more complicated descriptive one, and to have no reason to explain it. I would also urge its general use.

A year ago when the subject of immunity to re-infection was brought more prominently into tuberculosis literature by Prof. Paul H. Roemer, one of the foremost German workers, but little interest was excited by it, judging from the lack of discussion on the part of the tuberculosis clinicians in Europe. Fortunately to my thinking, Drs. Hamman and Wolman have shown a thorough appreciation of its importance in their recent excellent work on "Tuberculin in Diagnosis and Treatment." More recently Col. G. E. Bushnell, of the Army Medical Corps at Fort Bayard, has also reviewed Roemer's and Hamburger's experiments and deductions as to primary and secondary infection.[2] The far-reaching import of these deductions warrants abundant study in both laboratory and clinic. Therefore, if some of my remarks seem like needless repetition of facts already familiar to you, I hope you may find enough angles of view to repay you for listening. I venture now to present some observations intended for your meeting on this date last year, when illness interfered with my attendance.

It has seemed to me that we have not generally appreciated the important bearing some of the earlier experimental work on tuberculosis in this country has on the problem of infection. We have become so accustomed to the current exaggerations about the danger from infection to adults as well as children, that we have overlooked strong proofs to the contrary. If we can now marshall facts, both experimental and clinical, to disprove some of the popular teaching in reference to infection, I believe a great service can be done for the prevention of cruelty to consumptives. It ought to allay fears of contagion to some extent at least, and there is a duty for public authorities in this connection.

For the sake of clearness, I shall define at the outset my understanding of the word "allergy" as applied to tuberculosis. It should include all forms of tuberculin reactions, whether local or general, or any inflammatory process caused by tubercle bacilli or their products after infection has been established. It should then be a very comprehensive term, covering practically all manifestations of the reactions between the tissues and the disease agent.

It is well established that after primary infection, it requires 10 to 15 days to develop the allergic state. Up to that time the infection has aroused but little response in virgin soil. Then follows an inflammatory stage, fever develops, and local changes announce the fact that tubercle bacilli have called forth a specific change. Henceforth the individual responds differently to a subsequent exposure. The minute studies of v. Pirquet are so familiar that it is unnecessary to review them. The course of tuberculin skin reactions abundantly demonstrates the principle, and it is of course schematic for many other forms of allergy. What I wish to refer to in particular is the intimate nature of the reaction and its apparently protective function as related to re-infection in tuberculosis.

Nature of Tuberculin Reaction.—As is generally accepted at present, tuberculin reactions are evidences of tuberculo-protein hypersensitiveness. My associate, Dr. Krause, presented before this society two years ago a review of our work at the Saranac Laboratory on this subject. He has since extended it with interesting results, some of which bear on the problem of re-infection and will be referred to later. There has been a tendency to doubt the propriety of considering the tuberculin reaction as closely related to other forms of foreign protein sensitiveness. This was mainly due to the inability to sensitize normal animals with tuberculin and elicit anaphylactic death or symptoms similar to those produced by other proteins in sensitized animals. In some of my earlier work the results were negative or inconclusive, but later we succeeded in obtaining positive anaphylaxis with crude tuberculin, or a similar glycerine extract of the bacilli, as well as with the pure protein extracts.

On the other hand, there are features of the tuberculin reaction not closely paralleled by other protein-sensitive reactions. There are the focal and cutaneous reactions, the auto-tuberculin effects excited by hyperemia of a tuberculous focus and also those produced in highly sensitive tuberculous subjects by heterologous proteins, such as beef albumose or other bacterial proteins.

Through the complete correspondence that we have found to exist between the anaphylactic reactions of tuberculo-protein and those of other proteins, we have felt that here the key to all the reactive phenomena of tuberculosis should be found. This is doubtless true but not easily demonstrated. The problem of creating skin sensitiveness, for example, without producing a tuberculous focus in an animal has engaged my attention for some years.[3] Thus far I have not succeeded either by the use of the tuberculo-protein alone or mixed with the various waxy substances extracted from tubercle bacilli. The bearing of this

[1] Paper read before The Laennec, a society for the study of tuberculosis, The Johns Hopkins Hospital, April 28, 1913.

[2] *The Military Surgeon*, January, 1913.

[3] Studies from the Saranac Laboratory, 1900-1904, 1904-1910.

point on the subject in hand will perhaps be more apparent later. Now, with many other proteins it is quite possible to create a specific skin sensitiveness, *e. g.*, beef serum, but it seems to require the presence of actual tubercles in the animal before cutaneous reactions to the old tuberculin or the pure protein extracts can be elicited. A collection of powdered animal charcoal saturated with tuberculo-protein and placed under the skin or in the peritoneal cavity as a depot or storehouse has failed in my hands to create skin sensitiveness. The addition of the fatty substance extracted by benzol was also unsuccessful.[4] Similar experiments were made independently by Stocker, an assistant of Prof. Sahli, and are mentioned in the last edition (3d) of Sahli's Tuberculin Treatment (1912). He employed Beraneck's tuberculin in an insoluble precipitate, but without success in creating sensitiveness.

Thus far I have referred to sensitization with filtered extracts of the tubercle bacilli as a means of sensitization. When intact, dead bacilli are injected in sufficient numbers, skin sensitiveness appears and disappears with the formation and absorption of the tubercles thus formed (as you know, tubercle formation is readily produced by either dead or living bacilli), hence the inference that the tubercles are essential to this reaction. Further, it might be supposed that intact bacilli were also essential. This is apparently possible also, though experiments in sensitization with pulverized bacilli have shown slight skin reactivity.[5] In these, however, the presence of a few intact bacilli and the formation of temporary tuberculous tissue were not excluded. The same criticism may be made of the attempts of Much & Loeschke[6] to create tuberculin reactivity with bacilli dissolved by lactic acid, neurin, and other solvents. Tuberculous foci are often too minute to be discovered by the most careful post mortem examination, and I am compelled to think that all experiments in immunity against tuberculosis where the tuberculin fever and skin reactivity have been established, can be explained in this way. I refer to the bovo-vaccination of v. Behring and Roemer, Koch, Heymanns and v. Baumgarten, as well as the earlier experiments of Trudeau, and Pearson and Gilliland in this country. Not only the tuberculin reactivity but the immunity acquired by the animals is explained by the presence of tuberculous foci produced by the vaccine. It is true the tubercles are not always discoverable nor are they necessarily permanent lesions when the vaccine used is of low virulence, yet it has been found that the best relative immunity thus obtained persists no longer than the allergic state of the animal, or in other words, until the complete disappearance of the vaccine or obliteration of the foci caused by it.

We are brought to the conclusion that the immunity acquired by vaccinated animals rests upon the presence of tuberculous tissue. Roemer[7] is not sure of the identity of the allergic reaction to re-inoculation with the reaction to tuberculin, because the latter may be absent in animals who show a marked hypersensitiveness to a new infection. Moreover, he calls attention to the fact that by treatment with dead bacilli tuberculin allergy can be produced, yet no perceptible immunity developed. While the reason for these differences in reaction is not easy to explain, I think it is a mistake to think that the mechanism is at all different. One suggestion is that the dose of tuberculin or bacilli used, as well as the manner of administering it, may govern the result of a test in a vaccinated animal, whether positive or negative. It is too much to assert this, but allowing for varying degrees of susceptibility there is much to support it. It is quite true that calves and rabbits may lose all reacting power to moderate doses of tuberculin after vaccination, and yet when re-inoculated respond with a sharp allergic reaction. The absence of tuberculin allergy in these cases is probably more apparent than real, only the dose may not be large enough to arouse fever. I do not know of intravenous tuberculin tests being made in such animals. The sum of all our observations is that relative immunity in tuberculosis is associated with the allergic state, either active or latent, and this passes away gradually with the disappearance of the primary vaccination or infection.

There is, nevertheless, one allergic reaction that may never be wholly lost during life, once sensitization has occurred. This is the capacity for anaphylactic shock, and it seems to persist quite irrespective of the focal and febrile reactions. Neither does an animal show any perceptible immunity from experimental infection if only sensitive to anaphylactic shock (Krause[8]). Possibly the limitations of experiments on guinea pigs may account for the negative results, but certainly a high degree of immunity can be induced in these animals by inoculations of bacilli attenuated in virulence and which lead to a delicate allergic sensitization.

It is natural to enquire into this difference and its cause. I have no theory to offer except to again call attention to the importance of the focus containing the bacilli as contrasted with the sensitization with soluble products of the bacilli, possibly altered by the simplest manipulations so as to lose some element of importance. More than likely the difference is merely in degree. The focus is to be considered as a collection of cells more highly "trained" (if one may use an athletic term) to react, because in continuous contact with the bacilli. It is less easy to account for the tissues being sensitized that are not in direct contact with the bacilli. These are suggestive fields for experiment.

From what has been said it is implied that any actual infection with tubercle bacilli produces a certain amount of protection against subsequent infection; at least while the allergic state persists.

Super- and Re-Infection.—It will be well here to distinguish between "super-infection," or "additional" infection, which predicates the existence of active or latent disease, and "re-infection," occurring after clinical healing of a pre-existing

[4] Investigations into the Nature of Tuberculin Sensitiveness, Transactions of the Seventh Annual Meeting National Association Study and Prevention of Tuberculosis, 1911.

[5] Studies from the Saranac Laboratory, 1904-1910.

[6] Much & Loeschke: Beiträge z. Klinik d. Tuberk. XX, 409.

[7] Beiträge z. Klinik. d. Tuberk. XI, 130.

[8] Studies from Saranac Laboratory, Jour. Med. Research, 1911, XXIV, 361.

tuberculosis. In making such distinctions it must be remembered that there can be no hard and fast line drawn between clinical healing and latency. In both cases tuberculin allergy persists so long that this test cannot be used as a criterion of healing in the human subject. In the bovine race the same holds good in relation to natural infection. The real problem is to determine whether this allergy is dependent on the extent of the original infection, its incomplete healing, or upon a true re-infection, whether from outside sources or from auto-re-infection. It is well known that an encapsulated tubercle of small extent, and to all appearances healed in the clinical sense, may yet be the only discoverable source of a positive tuberculin reaction. It is also true that the delicacy of the reaction is usually in inverse proportion to the age and in direct proportion to the extent of the healed focus. In many persons in adult life this is probably the reason for the delayed or feeble response to the cutaneous tests, as v. Pirquet and Wolff-Eisner have explained. It requires repeated subcutaneous or even intravenous tests to make certain that some degree of allergy is not present. This is, however, of little practical importance. What we wish to know is, how much value the primary infection is to us as a protection, and if the allergy is always a desirable condition. The experiments of Koch, Trudeau, De Schweinitz, v. Behring, and many others on guinea pigs, rabbits, cattle and sheep clearly showed, when interpreted in the present aspect, that it was a protection. The more recent ones of Nichols[*] in our laboratory can now be interpreted in the same light.

It is to Roemer and Hamburger that we are chiefly indebted for bringing forward direct experiments bearing on super-infection and also to Wolff-Eisner for emphasizing the principle. The first two workers showed that it was practically impossible to produce a second infection in guinea pigs already diseased with chronic tuberculosis. Roemer has tried intracutaneous, subcutaneous, inhalation and feeding methods in attempts at super-infection, and from these and all the preceding experiments of v. Behring and himself on vaccination against tuberculosis, he finds further confirmation of v. Behring's ideas of infection in early life and the relative immunity which follows a mild infection. He finds the course of the disease in adults and the types seen in different races to be best explained on the basis of these experiments. Without going into all the points of epidemiology and the question of paramount importance, the proportion of infections in early life, which Roemer considers at length, I desire to touch only the aspect of re-infection or, as it must be in many cases, super-infection. At the start it is to be remembered that the immunity above mentioned is only relative, not absolute, and yet it may be very effective. We know that the bodily resistance is fluctuating and dependent upon numerous factors. In animal experiments with tuberculosis we cannot imitate or parallel all the human conditions, so we are obliged to infer from clinical evidence that resistance to tuberculosis varies widely at times and is frequently broken down. It is harder yet to discover that a new development of the disease is a re-infection from outside when an autogenous source is easily possible.

[*] Nicols, J. L.: The Medical News, 1905, LXXXVII, 641, 653.

We are obviously confronted by many puzzling possibilities. For convenience, we may divide the population into four classes: *First*, those who never have received a tuberculous infection and hence do not react to tuberculin. They are mostly under the age of ten. *Second*, those who have received a very slight infection, in quantity, virulence or both. This includes a large number of healthy adults who may or may not react to tuberculin. *Third*, those who received an infection sufficient to produce symptoms of disease, either latent or progressive. Many of this class will be found in tuberculous families. They will usually react strongly to tuberculin. *Fourth*, those who received a primary virulent infection progressive and fatal.

We shall readily see that many of the first class will become infected as they grow older, until practically all will sooner or later react to tuberculin. Next we shall have to assume in the light of the experimental observations that all the infected classes acquired some specific immunity at the time of their infection. In the last two classes one can hardly expect a superinfection from outside sources, knowing the much greater probability of auto-infection. The agencies that would make for reduced resistance to exogenous infection would also encourage autogenous super-infection.

The greater second class is the one most liable to exogenous re-infection, and the great majority of them must be exposed from time to time to it. While they are in good health and continue to show tuberculin allergy, it is very likely that they will resist exogenous infection by inhalation or swallowing. If inoculation accidentally occurs as in many pathological students, or purposely as F. Klemperer and C. Spengler have done on themselves, we know that the infection remains localized usually in the skin or nearby glands. The bacilli do not die, or at least not all of them, and even in Roemer's and Hamburger's experiments were found to be virulent, though apparently restrained from further growth.

It is of interest to know what would happen to an individual who has apparently lost the tuberculin allergy in the lapse of time, and while in good health inhales tubercle bacilli. We have no answer to this from the experimental side, except in bovine vaccination, yet we can pretty surely predict that no infection will take place in the majority. As soon as the bacilli shall obtain lodgment in the tissues, the old allergy will quickly return and localize if not destroy them.

Anergy.—We must go further and enquire what will be likely to happen to individuals who have lost tuberculin allergy from disease, as is known to occur in measles and scarlatina. I refer to the observations of v. Pirquet and others where no response occurs to the tuberculin cutaneous test during the height of the disease. Here again it was found to return after convalescence and could hardly fail to act in the event of exogenous infection. Outbreaks of tuberculosis during convalescence from other diseases are not easily associated with recent infection in the sense that exogenous bacilli were implanted during or after the illness. More often, as we know, the bacilli were already present in the lymph glands or old nodules from a previous infection. During the condition of "anergy," as ex-

plained by v. Pirquet, the bacilli may be scattered and create new foci when allergy returns. Of course we are in danger of taking a too narrow view of infection if this is our only explanation of the mechanism. Undoubtedly, the hyperemia around the glands at the root of the lung furnishes mechanical conditions of great importance in certain diseases like measles and influenza. Here we have a tuberculin-like focal reaction at an unfavorable time. With it doubtless there may be a loss of protective functions, such as digesting ferments, antibodies, and leucocyte activities, such, if you please, as opsonins. I think we should class all those which act specifically against tubercle bacilli as "ergins" in possibly a broader sense than the word is used by v. Pirquet. This would not prejudice any theory as to the relative importance of the specific substances, but it has the advantage of comprehending all of them.

When the allergic state is restored, we should expect a different pathologic picture in the spreading tuberculosis than in a primary infection. This is in fact the case according to many observations. The marked infiltrations in the lungs, pneumonic consolidations in reality, are accounted for by the strong allergic reaction. The contrast between these and miliary tubercles is very evident, and can be demonstrated experimentally (Nichols [10]). The development of a strong allergy in previously infected individuals is at least one reason why miliary tuberculosis is not more frequent during relapses and extensions of the disease. The recent discovery of bacilli in the circulating blood, more frequently than formerly thought possible, adds to the belief that some powerful protection exists to overcome them. This has been especially noted by v. Behring and Roemer.

That miliary tuberculosis is accompanied by anergy has been proven by v. Pirquet. Acute pneumonic tuberculosis also leads to this state when cachexia develops, but the lesions undoubtedly antedate the failure of reactive power. Weakened allergy occurs after tuberculin treatment, but this is not necessarily a sign of weakened resistance, nor is reaction power wholly lost; it is only in abeyance as shown by occasional high fever reactions when the dose of tuberculin is increased enough. Wolff-Eisner,[11] however, argues that this tuberculin treatment anergy is favorable to further infection.

Having found so many ways in which the bodily resistance is broken down and tuberculosis develops, we would enquire whether simple overwork, worry, underfeeding, injuries, and the like are accompanied by anergy. If so, will it permit exogenous infection? I do not know of any studies on the tuberculin reaction from this point of view. In large series of tests, like those of Beck [12] and Franz,[13] it is hardly probable, as least, that the large percentage of positive-reacting individuals were all in good condition when tested. It is also certain that many persons in very bad physical condition, who suffer from overstrain as well as latent tuberculosis, react strongly to tuberculin. Moreover, it is certain that the disease often spreads under these conditions from the primary source. To account for this, it has been thought by some that auto-infection was more dangerous than exogenous, because the bacilli were adapted, as it were, to the individual. Roemer's [14] attempts to reinoculate guinea pigs with their own bacilli, however, were not successful by way of the skin, although the original disease was progressive. Finally, it has been shown, especially by Hamburger, that the super-infections tend to ulceration—if the dose be sufficient—at the site of injection. In natural infections, however, the exogenous bacilli are generally inhaled or swallowed, or both; and the question arises whether they can penetrate the allergic individual under any circumstances. I think it was Prof. Theobald Smith [15] who first suggested the possible cause of cavitation in the lungs to be the inhalation of bacilli of higher virulence than the first infection, which were held at the portal of entry, but were able to produce local damage. While this is one explanation, cavitation is often seen in animals with a long-standing chronic tuberculosis in which no question of secondary exogenous infection can be raised. Without facts to favor a theory of re-infection of a formerly allergic person, we can only admit that possibility. If possible at all, the conditions are likely to be extreme in number and virulence of bacilli.

On the other hand, there are some reasons to consider the lung parenchyma, especially in the apices, a place of lower resistance to tubercle bacilli than other external surfaces. If this is true, inhaled bacilli in adults are conceivably lodged in the alveoli, and as in Hamburger's experiments, may grow and produce surface ulceration in an allergic individual. It appears to be a field not satisfactorily covered by investigation. Super-infection with ulceration in the lungs is demonstrable, but according to all the experimental evidence it is autogenous.

What we most wish to know for the peace of mind of the public is under what conditions, if any, exogenous super- or re-infection occurs in the pulmonary area. The clinical literature of inoculation tuberculosis of the skin and mucosa is not very satisfactory in furnishing evidence of re-infection of the lungs. The surfaces are certainly all exposed but not to be compared. Furthermore, autogenous infection of the lungs is clearly the most common form from all experimental evidence as well as pathologic studies.

Most of the writers on tuberculosis have recognized the astonishing infrequency of laryngeal and intestinal super-infection in open tuberculosis. This refers of course to the individuals who still have good vitality, or, translated into the terminology here employed, efficient allergy. As the disease advances naturally a change takes place and the allergy reveals its paradoxical action; it is so exaggerated that harm results from the toxemia and ulceration. Here we have one rationale for tuberculin treatment, about which much dispute has arisen. It seems reasonable to attempt to lessen the high sensitiveness seen in many patients and in the scrofulous children particularly. I cannot follow Wolff-Eisner [16] in his belief that abolition of tuberculin skin and fever reaction leads to danger of

[10] *Loc. cit.*
[11] Frühdiagnose u. Tuberkulose Immunität, A Wolff-Eisner, 1909.
[12] Deutsche med. Wchnschr., 1899, Vol. XXV, p. 137.
[13] Wien. klin. Wchnschr., 1909, Vol. XXII, p. 991.
[14] Beiträge z. Klinik d. Tuberk. XVII, 316.
[15] Theobald Smith, J. Am. M. Ass. 1906, XLVI, 1253-4.
[16] *Loc. cit.*

further infection. The further we study these reactions the more they appear to be life-conserving rather than health-conserving. While we seem to be protected in ordinary exposure against a fatal miliary tuberculosis, tuberculous patients are slowly poisoned by the very mechanism of resistance overdeveloped or over-active. I do not press this point too far, or is it settled beyond doubt? It is enough to draw attention to the double-edged action of allergy.

In conclusion it seems pertinent to make some practical use of our knowledge of allergy in tuberculosis. If some things sound too speculative, and my deductions are pivoted on too small points, yet we are reasonably sure of some things. These are (a) that most adults have received some tuberculous infection; (b) that a variable degree of specific allergy is thus acquired; (c) that during ordinary health the tissues repel tubercle bacilli, partly with the aid of specific allergy; (d) re-infection is mostly autogenous super-infection and due to disease, overstrain, trauma, or any cause of lowered vitality, whatever that may mean. Finally, (e) as a corollary, adults are very little endangered by close contact with open tuberculosis, and not at all in ordinary association. Childhood is the time of infection, youth the time of super-infection, and that from extension of the primary disease.

Qualify these statements as we may, it is time for a reaction against the extreme ideas of infection now prevailing. There has been too much read into the popular literature by health boards and lectures that has no sound basis in facts, and it needs to be dropped out or revised. More protection of children and better hygiene for adults are logically demanded, but beyond this the preachments about the danger of infection to adults in the present state of society are without justification from an experimental standpoint. Deductions from case histories must be accepted with much doubt, when circumstantial evidence is presented showing the source of infection to be recent exposure in adult life.[17] This is particularly applicable to the question of hospital and dispensary contact for nurses and resident staffs. It also applies to alleged infection of married partners, already the subject of careful investigation, without producing satisfactory proof of infection (Weinberg,[18] Pope and Pearson [19]).

Phthisiophobia has had no check from the time the knowledge of the bacillus was popularized. Cornet's dust experiments first gave the impulse to a fear, followed by Flügge's droplet infection, which has aggravated the solicitude felt by physicians and nurses and which has been gradually spread to the laity. Not until the researches that I have briefly laid before you have we had much to show the way to a more correct judgment of the real danger to adults.

[17] Bruck and Steinberg (Ztschr. f. Hyg. u. Infectionsk., 1912, LXXI, 177) conclude that 31 per cent of cases studied by them were classed as such. They admit the lack of proof.

[18] Beiträge z. Klinik d. Tuberk. 1906, v.

[19] Draper's Company Research Memoirs III, 1908.

PROCEEDINGS OF SOCIETIES.

THE JOHNS HOPKINS HOSPITAL MEDICAL SOCIETY.

February 17, 1913.

Dr. Thomas S. Cullen presiding.

Myelogenous Leukæmia treated by Benzol. Dr. L. F. Barker and Dr. J. H. Gibbes.

This gentleman, a private ward patient who is kind enough to come down here to-night, is 57 years of age. He entered the hospital November 23, complaining of nervousness and general debility. The family history is negative.

In March, 1906, he was treated in this hospital for neurasthenia and left the hospital comparatively well. He continued to feel well until two months before his present admission, when he began to have feelings of general insufficiency. On physical examination no abnormalities were found. He was referred to one of us by Dr. Randolph of Charlottesville, Va., on account of the marked increase in the leucocytes of his blood. Examination showed a red blood cell count of 3,600,000; white blood cells 360,000; hemoglobin 79 per cent; the stained smears and differential count yielded a typical picture of myelogenous leukæmia. The spleen was not palpable. The Wassermann reaction was positive. X-ray of the long bones was negative. The urine contained hyaline casts, and a small amount of Bence Jones body (Dr. Guthrie).

The results of treatment with a new method (benzol) have been so remarkable that we felt that the patient should be seen by the members of this society.

The method of treatment used during his stay in the hospital was as follows:

From November 24 to 26, no treatment was given. On November 26 Fowler's solution, beginning with 3 minims and increasing, was ordered. On November 26, 1912, the white count was 250,000, and on December 5, 1912, 192,000. After five days a single dose of neosalvarsan was given, and on December 10, 1912, the count was 210,000. Benzol was now begun and the Fowler solution stopped.

The origin of the benzol treatment is of interest. You may recall that some three years ago, three girls who had been poisoned by benzol in a factory in Baltimore, entered the medical clinic of this hospital for observation and treatment. They had been severely poisoned and developed anæmia and purpura hemorrhagica, two of the cases ending fatally. Dr. Selling, who studied the tissues in Professor Welch's laboratory, found an extensive aplasia of the bone marrow of these patients. Since Dr. Selling's studies, considerable experimental work has been done in the pathological laboratory here by Dr. Winternitz and his associates. It is interesting that the therapeutic application of benzol grew out of the studies of Dr. Selling. Professor von Korányi, in Budapest, noticed the studies of Dr. Selling and thought it might be well to try benzol in the

treatment of leukæmia. The effects were remarkable. He has kindly sent us reprints of his articles and we have used his method in treating this patient, with good results.

We have seen that on December 10, before benzol was started, the white cell count was 210,000. After five days of benzol, that is on December 15, the count was 184,000; this represents relatively little change, not more than had been taking place before the administration of benzol. On December 25, the count was 170,500—very little diminution. It was Professor von Korányi's experience that in the first three weeks of benzol treatment, very little change in the white count is observable. On January 25, the count was 98,000—a definite drop. On January 30, it had fallen to 48,000 and on February 13, to 14,200. The hemoglobin, as you see, is 71 per cent now, contrasted with the 65 per cent shown when he came in. Benzol, in suitable doses, seems to stimulate the erythropoietic marrow while it reduces the leukopoietic marrow. We have stopped the benzol now because it has been observed that the diminution in the number of the white cells goes on after benzol is stopped and we do not desire to cause too much hypoplasia of the marrow. The differential counts of the white cells in the course of the treatment are interesting and will be given in detail when the case is reported in full. The results obtained with this patient make us feel sure that there will soon be a general interest in the treatment of leukæmia by benzol. It is, of course, far too soon to pass judgment upon the real value of the treatment.

The substance should be most cautiously employed to avoid benzol poisoning. It would probably be wise to limit its use at present to hospitals in which close watch can be kept over the patient's condition. Dr. Frank Billings, of Chicago, has recently reported several cases treated with benzol, and several articles on the subject have already appeared in European literature.

The Statistical Experience Data of The Johns Hopkins Hospital, 1892-1911.* FREDERICK L. HOFFMAN, Statistician, The Prudential Insurance Company of America, Newark, N. J.

DISCUSSION.

DR. H. M. HURD: I am sorry that Mr. Hoffman has not seen the tables which were prepared many years ago in connection with the Michigan State Hospital for the Insane at Kalamazoo.

I became connected with that institution in 1870, and one of my first occupations was to tabulate what had happened to one thousand selected insane patients. Tables were prepared containing the names, ages, forms of insanity and the termination of treatment in these cases, that is whether they had recovered, improved, died or were remaining in the institution. The form of tabulation proved so instructive that in 1872 it was adopted as a form for statistics, and for a number of years, at least as long as I remained connected with the institution, these tabulations were used.

When I removed in 1878 to Pontiac, Michigan, where I opened the Eastern State Hospital, I adopted the same form of tables and published them annually until 1889, when I removed to Baltimore. Here the question of statistics soon after opening the institution again came up, and after consultation with Drs. Welch and Billings, it was decided to adopt the form of table which had already been used in Michigan.

It was thought best in view of the varying morbidity and mortality of the white and colored races to make separate tabulations for them, a casual study of the health statistics of the city of Baltimore having shown the death rate among the white patients to be about 20 per cent, and that of the colored race about 33 per cent.

I did not then fully realize the value of these tabulations because I was not a statistician, but I hoped that some good would come out of it. These tables have been continued for nearly 24 years, and I am gratified that at last all appreciate the advantages which may come from their use.

As to the dispensary tables, I can only say that there are some difficulties in connection with dispensary work, owing to the fact that many patients only come to the clinics once or twice and if the disease is at all obscure, it is difficult and well-nigh impossible for a conscientious medical man under the circumstances to make a definite diagnosis. For this reason in many services the list of forms of diseases has been imperfectly filled out and under the heading "Unascertained" a large number have been classed. I hope that with better methods in the dispensary and an increased amount of medical assistance it may be possible to improve the character of the dispensary statistics.

DR. L. F. BARKER: Dr. Osler is always urging that we appoint a thoroughly trained statistician to the hospital, and I hope that this meeting to-night may stir us up to make arrangements for a first-class man to work here all the time. It was gratifying indeed to hear such an appreciative statement as Mr. Hoffman has made regarding the statistics as kept thus far. I was much interested to see how clearly he had put his finger on certain peculiarities of our work, merely from his study of these statistics; it is certainly striking that a man from outside, who has no actual knowledge of our local conditions, should be able, by his consideration of the statistics alone, to pick them out. Local conditions should, of course, always be kept in mind in attempting to interpret the significance of statistics. For instance, in drawing deductions regarding the relative number of admissions for race and sex one should know the whole number of beds provided for white men and white women in each service, and the number for colored men and colored women, or he might be seriously misled. Again one should know how many "pay" and how many "free" patients there are. Again, the duration of the hospital stay varies greatly for patients suffering from different diseases. The relatively small number of cases of certain diseases treated in this hospital may throw no light on incidence, but be due to lack of provision for, or of special interest in them. For instance, the small number of "tuberculosis" admissions was pointed

* To appear in full as a monograph of The Johns Hopkins Hospital Reports.

out. Thus, patients suffering from outspoken pulmonary tuberculosis are not admitted here; only occasionally a case slips in unrecognized until after admission. The hospital is used mainly for the treatment of acute, rather than of chronic, diseases. If chronic cases are admitted, it is usually for a brief period of observation and diagnosis rather than for prolonged treatment. That alters the whole statistical picture. This feature is well illustrated in comparing surgical with medical admissions. A surgical ward is largely an institution for therapy, but a medical ward has to be, at present, to a large extent, an institution for diagnosis; and this influences the statistical results very definitely.

The speaker had a good deal to say about the "morbidity" of a large city like Baltimore. Regarding this, inferences should be drawn only with great caution from our statistics. Consider just one point: the colored wards draw chiefly from the city, the white wards chiefly from outside of the city. The public wards for white patients and the private wards of this hospital draw from the country at large, and so any statistical deductions regarding morbidity in the city would be fallacious unless this fact was especially considered in the tabulations.

Similarly, the comparison of the mortality rate of white and colored people for a given disease might seem to be fair in a hospital in which the colored people are treated and studied just as carefully as the white people; but, nevertheless the conditions are different for the two races. The colored people do not come into the hospital until they are absolutely compelled to and often cannot get in unless they are very seriously ill, whereas more white people can enter as pay or part pay patients, and thus enter for milder maladies than do the colored. Anyone who knows wards M. and O (the colored wards) has been struck by the number of patients suffering from aneurysm and from cardiovascular diseases. Many of them enter shortly before "exitus"; for humanitarian reasons it is necessary for us to care for them, while many of our white people with similar diseases can be well cared for in their homes. Again, while Wassermann reactions are common in both the colored and the white wards, still the proportion of positive to negative reactions is much higher in the former than in the latter. If our statistics indicate as they do that the mortality among the colored men entering the hospital is much higher than that among the white men, we must remember that a whole series of conditions have to be considered in order properly to interpret the fact. It is instances like these which emphasize the importance of a statistician constantly working in the hospital, and familiar with all the peculiarities of our local conditions.

Take another example to which Mr. Hoffman referred: the mortality statistics for malignant diseases among white men and white women. When the mortality statistics in men and women suffering from malignant disease are quoted, very different groups of diseases are under comparison. "Malignant disease" in men is very different from "malignant disease" in women. If you analyze the surgical diagnoses of malignant disease in women you will probably find that they consist, in large part, of cases of carcinoma of the breast, of the uterus, and of the stomach. In men, a similar analysis will probably reveal predominantly cases of carcinoma of the lip, tongue, œsophagus, stomach and rectum. I am speaking wholly from impression but I am very sure that the incidence of malignant diseases in men and women would be very different for the several organs, so that in comparative statistics, unless one choose a given malignant disease of a given organ rather than merely malignant diseases as a whole, deductions are sure to be fallacious.

I say these things, not at all in criticism of anything that Mr. Hoffman has said, but simply to emphasize the great importance of a full knowledge of local conditions for the proper keeping and valuation of hospital statistics. Each of us connected with the hospital must always be grateful for the great service Mr. Hoffman has rendered us in these careful studies of his and for pointing to the way we should follow.

Dr. W. H. Smith: I don't think I have anything particular to add to what has been said. It is always interesting to note the free and easy manner in which recommendations are made for the appointment of additional workers. I wish it were as easy to find the money with which to pay for them.

While Mr. Hoffman was speaking of the great value of statistics, it was brought to my mind that in the last few years the question of hospital statistics has more than once been up for discussion in the meetings of the American Hospital Association. The authorities of some hospitals have maintained that the statistics published in the annual reports were useless and might well be eliminated. Some hospitals have discontinued publishing such statistics. From what Mr. Hoffman has said it is possibly just as well that they have done so. If I understood him correctly the published statistics in the majority of hospital reports are of very little value. It is an interesting and remarkable fact that practically no two hospitals use the same terminology in tabulating their statistics relating to diseases. There is no uniform nomenclature. In this hospital some work has been done by Dr. McCrae and others, but it has never been satisfactorily completed. I happen to have been a member of a committee of the American Hospital Association which reported at the last annual meeting on the subject of uniform nomenclature for hospital publications. The committee, after conference with various authorities, among others Mr. Cressy L. Wilbur of Washington, recommended the adoption of the Bellevue Hospital nomenclature. The most extensive work along this line has apparently been done by the Committee of Records at Bellevue. Dr. Warren Coleman and Dr. Robert Carlisle have been the chief workers. They have worked for the last eight or ten years in bringing out a small volume known as the Bellevue Hospital Nomenclature. It has been revised two or three times, the last revision having appeared about two years ago. At that time their work had been brought into conformity with the International Classification of Causes of Death, and in it appeared for the first time a very valuable classification of industrial diseases.

There is still much work to be done along this line. I mention this, because many of you here will be going out to other hospitals in various parts of the country and will have your

opportunity to contribute something to the better development of hospital statistics.

DR. F. L. HOFFMAN: I am glad indeed that some additional points have been raised in discussion which, on account of the limitations of time, could not be included in my address. As regards resident and non-resident patients, it is unfortunate that this distinction should not appear in the annual reports, but it would obviously be a most difficult matter to fully account, in all the required details, for the admissions and mortality by the residence of the patients. I may say in this connection that there is a table included in my address which shows that in proportion to population the number of deaths in Baltimore hospitals, according to residence, was as follows: resident whites, 16.7; non-resident whites, 7.0; resident colored, 32.6; and non-resident colored, 8.3. These rates are per 10,000 of population, and they would hardly sustain the point raised that a much larger proportion of non-resident whites are treated in Baltimore hospitals than non-resident colored.

As regards the duration of treatment, I regret that there is no information contained in the annual reports other than a table giving the average duration for all causes, which is stated to be 22 days. This table I have included in the Statistical Appendix to my address, together with some financial data as regards the cost of treatment.

Concerning the details of cancer by organs or parts of the body affected, I regret that for want of time I could not enter into a full discussion in the course of my remarks, but in the addresses as it will subsequently be published every form of cancer is given in detail, together with the death rate, whether medical, surgical, or gynæcological, so that every combination of facts can be made as desired. If I had gone into the details of cancer mortality there would have been no end to this discussion, but all the facts are contained in the Statistical Appendix to my address.

I have been particularly pleased with what has been said by the former superintendent of Bellevue Hospital, and I sincerely hope that the Bellevue classification of diseases will hereafter be used by the Johns Hopkins Hospital, instead of the present and more or less antiquated and misleading one. It is much on account of the cumbersome classification that I have not been able to complete my analysis by diseases, since quite frequently the same diseases are reported under different terms. The classification used does not admit of comparison with others, and if you want to aid in the effort to bring about uniformity in nomenclature you cannot do better than to adopt the Bellevue classification.

What has been said with reference to the tendency on the part of hospitals to eliminate from their annual reports the desired statistical account of the hospital experience, I cannot but feel is most regrettable. I, however, am inclined to think that if hospitals do not of their own account publish full returns concerning their experience, sooner or later the government will insist upon a full accounting for what is unquestionably a most important public function. In this respect the demand will not be for less but for much more information, just as there is an increasing demand for publicity on the part of corporations and other business concerns. In any event, Johns Hopkins Hospital stands in the front rank of publishing annually the kind of reports which should be made public by all American hospitals, regardless of size or class of patients treated, whether public or private, and I sincerely hope that my address will aid in bringing about this much to be desired result.

March 3, 1913.

Dr. Thomas S. Cullen presiding.

The Treatment of Syphilis of the Nervous System with Especial Reference to Tabes Dorsalis. DR. ARTHUR ELLIS, Rockefeller Institute, New York.

DISCUSSION.

DR. L. G. ROUNTREE: In listening to the papers of DRS. Ellis and Keidel I have been tremendously impressed with the close analogy existing between syphilis and trypanosomiasis, more especially in regard to their failure to respond perfectly to treatment. In trypanosomiasis the same four possibilities as to the reasons for failure of treatment, *e. g.*, relapse, have to be considered, viz., *festigkeit*, difference in individual resistance, inaccessibility of the organism to medication and the possibility of a life cycle in some stage of which the organism resists the action of drugs. *Festigkeit* is not the primary cause of relapse, since this cannot play a rôle until several treatments have been administered, and relapse occurs after the first treatment just as it does after the twentieth. Also, relapses in trypanosomiasis occur after treatment with sodium antimony thioglycollate toward which *festigkeit* could not be demonstrated.

There are probably other areas of the body beside the cerebrospinal canal and central nervous system which serve as sheltering or protecting areas during drug therapy. The bone marrow extracts of treated trypanosome animals give frequent successful inoculations when extracts from many other tissues fail.

Terry has recently shown that incubation of atoxyl serum at certain temperatures increases its toxicity for trypanosomes. The explanation of this fact is not yet apparent.

DR. H. M. THOMAS: I have listened to the paper of Dr. Ellis with extreme interest. I have been so fortunate as to have had the opportunity, when visiting the Rockefeller Institute from time to time, of seeing Dr. Ellis and Dr. Swift at work, and I have been impressed, as I am sure every one must have been, by their skill and accuracy. The tables that Dr. Ellis has shown us in themselves demonstrate this.

As he was speaking I could not help thinking of the various stages of development through which our knowledge of the relationship between syphilis and tabes had passed during my own interest in diseases of the nervous system—now more years than I care to recall. At the beginning of this time Fournier in Paris, Erb in Heidelberg, and Gowers in London, had just called attention to the probable causal relationship between syphilis and tabes—a view that at that time was quite novel. One of the chief criticisms of this view by its opponents was

that anti-syphilitic treatment appeared to have no result on the development of tabes; indeed, the idea was advanced by some that tabes was actually caused by the effects of mercury on the spinal cord. However, ever since the hospital was opened all our cases of tabes have been consistently and thoroughly treated by the anti-syphilitic methods in use at the time, with what result, of course, it is difficult to say, but we have seen a number of cases in which the process has remained practically stationary during many years, and in some cases remarkable improvement has occurred. Anyone who has had much experience with the treatment of tabes knows how hard it is to estimate from the mere clinical phenomena what has been accomplished, and it will be the greatest boon if it turns out, as seems probable, that the laboratory study of the spinal fluid does give us reliable data. I should like to ask Dr. Ellis what is the longest time that the spinal fluid has remained normal in his cases.

Dr. J. T. Geraghty: Whatever may be the explanation for the failure of salvarsan to cure syphilis, there are several practical points which our experience with the drug during the last few years has brought out.

In the first place, the importance of seeing and treating patients in the early stage should be emphasized. It is our experience, as well as that of others, that those who present themselves in the primary stage, with a chancre only, and a negative Wassermann, can be completely and permanently cured by one or two injections. In the secondary stage, repeated injections of salvarsan combined with a vigorous course of mercury, should be employed. The amount of treatment necessary will have to be judged from past experiences, as well as from observations upon the blood. Quite a few of these patients with early or late secondary syphilis receiving repeated injections of salvarsan combined with intramuscular injections of mercury, have been under observation sufficiently long to believe that they have been cured. In the latent and long-standing cases the results with the salvarsan therapy have been most disappointing. It is extremely doubtful if salvarsan can completely cure a larger per cent of the cases in this class than were formerly cured by mercury.

Dr. A. G. Rytina: The work of Drs. Ellis and Swift opens a new and important field in syphilis therapy. Those of us who treat many cases of syphilis by salvarsan, know that the chances of a radical cure thereby depends largely on the time that we carry out radical treatment after the onset of the infection. The reason for the many failures of salvarsan in the later stages of syphilis is not due to any lack of specificity of the drug for the spirochæta pallida, but may be explained by the pathologico-anatomical changes present in syphilis after it has lasted some time. In chronic syphilis the spirochætæ become deposited in the form of incapsulated rests and often in parts of the body inaccessible to the circulation. Following salvarsan administrations, the vast majority of the spirochætæ are destroyed, but the few escaping may later on generate a new progeny and be responsible for recurrence of symptoms, etc.

It has been shown by Wechselmann that the cerebrospinal fluid may show a positive Wassermann reaction even before the onset of secondaries and while the blood is still negative. Now the work of Ellis and Swift and others has shown that the ordinary drugs, used in the treatment of syphilis, such as mercury, potassium iodide and salvarsan, are not excreted at all, or only in very minimal amounts in the cerebrospinal fluid.

It has occurred to me that if a routine examination were to be made of the cerebrospinal fluid, as well as the blood, in all cases of suspected lues, and if those individuals presenting a positive Wassermann in the cerebrospinal fluid were given the direct intraspinal treatment, as well as the general treatment now employed, it would be possible to greatly lessen the percentage of parasyphilis cases, as well as cause a larger number of permanent and radical cures. Is it not possible that the spirochætæ, when they get in the cerebrospinal system, are free from therapeutic attack, and not only capable of setting up lesions of cerebrospinal syphilis, but of sending their progeny to other parts of the body to cause future recurrences, etc. This is all theory and may be worth very little.

I would like to emphasize the point brought out by Dr. Geraghty, viz., the necessity of seeing these cases early and putting them upon prompt and vigorous treatment. I try to impress upon my students the importance of an early diagnosis by the demonstration of the spirochæta pallida and the need of instituting vigorous treatment, before the onset of secondaries, or the appearance of a positive Wassermann reaction. In the last few months I have administered neosalvarsan in 12 to 24 cases of primary syphilis by the multiple injection method. None of these patients have developed secondaries, and in all the Wassermann reaction is negative. How long this state will persist time alone will tell. I feel, however, that the future will prove that the majority of them have been cured.

Dr. A. Ellis: We have not had an opportunity of observing over any length of time cases whose spinal fluid has been reduced to normal. The spinal fluid of one patient has remained normal without any treatment for about four months. Whether these cases will remain normal or not is impossible to say, but probably some at least of them will relapse. In case such relapse occurs, they should, of course, have further treatment.

We have seen no indication of progress of optic atrophy in any of the patients under treatment. Several patients who have had a well-marked atrophy have had repeated intravenous and intraspinous injections. In most of these cases the color fields and visual fields have been repeatedly tested and in no case has any material alteration occurred.

Dr. Keidel has spoken about the variation of individual susceptibility. This variation plays an important part, I think, in the treatment of syphilis. One patient whom we have seen illustrates this very well.

This patient was treated from the beginning of the secondary eruption, with repeated injections of salvarsan and mercury. During the first year of his treatment he had 6 gm. of salvarsan and many intramuscular injections of mercury. At no time was he without treatment for longer than four weeks. In spite

of this, he had three clinical relapses. At the end of a year, on account of symptoms suggesting a possible meningitis, he was lumbar punctured and his spinal fluid showed 212 cells, a positive globulin reaction, and a positive Wassermann reaction. His treatment was then changed to neosalvarsan, and under this he rapidly improved and has now had a normal spinal fluid and a negative reaction of the blood for a period of four months.

In this patient neosalvarsan has seemed more efficient than the old salvarsan. This is in marked contradistinction to our general experience where we have found the old salvarsan very much more efficient. There is, apparently, an individual variation.

March 14, 1913.

Dr. Thomas S. Cullen presiding.

The Cultivation of the Virus of Epidemic Poliomyelitis. DR. SIMON FLEXNER and DR. HIDEYO NOGUCHI, Rockefeller Institute, New York.

The Presence of Treponema Pallidum on the Brain of General Paresis. DR. HIDEYO NOGUCHI.

DISCUSSION.

DR. ADOLF MEYER: It is not difficult to get one's enthusiasm stirred over a meeting of this kind. In a field like psychiatry where such a large variety of conditions confront one, it is a great comfort to feel that 15 per cent of these cases that we have to consider present problems which can be approached more and more definitely through the test tube, and that real helps in such investigations have been brought to us to-night. Psychiatry can be proud in this, that even with its apparently crude methods it has been able to single out of the supposedly confused mass of conditions such a clearly defined group and to assign it to the field of syphilis before even the spirochæta was known. I cannot help being reminded of an impression of one of my former associates, who had been an assistant in one of the largest hospitals in the country and who had watched with great interest the anatomical service of that hospital. He had come to feel that in general hospital work the anatomist was the one man who could have positively solid evidence under his feet, while the clinician was so frequently humiliated at the autopsy table with the shortcomings of his diagnostic means. In charge of the autopsies in our hospital for the insane he was strongly impressed by the fact that where the diagnosis of general paresis had been made clinically it was with surprising uniformity that the characteristic autopsy findings were established and the clinical diagnosis was substantiated by the post mortem studies. And that was before Wassermann came to our help. It was this field of psychiatry that freed him of a deeply rooted nihilism about the scientific strength of ante mortem pathology. From a neurological and in a great many instances the psychopathological point of view, it was possible to single out from among the many other forms of dementia the conditions which at the autopsy of the brain showed the cloudy œdematous pia and the adhesions to the cortex, the granulation of the ventricles and the infiltration of the cortical vessels with lymphoid and plasma cells, and which gave us the means of making a remarkably well-defined anatomico-clinical entity of parenchymatous syphilis. This most interesting observation of Dr. Noguchi distinctly opens to us an avenue of study which also was foreshadowed clinically, viz., the study of the question of why it is that in these conditions this widely present organism behaves in such a highly different way from what it does in other tissues of the body. It may also become possible to learn why it is that of 9 glass blowers infected from one source 5 developed locomotor ataxia or paresis, *i. e.*, what we called metasyphilis, or what we now should call parenchymatous syphilis, and whether it is possible to demonstrate a different strain of spirochætæ in the cases yielding "metasyphilis." It will now become possible to demonstrate the actual type of spirochæta present in the cerebrum and spinal cord. It will also become possible to try the findings of the Rockefeller Hospital where very successful efforts have been made in tabes to bring the therapeutic agents closer to the spirochæta through the cerebrospinal fluid. So far, general paresis has looked to us as a condition which can only be attacked by a vigorous onslaught against the spreading of syphilis in general. I have no doubt that that will remain the most important prophylaxis against general paresis proper, but where infections have occurred we are given at least some chance of obtaining, after experimentation, an accurate therapeutic means of attack. If we can hope to apply to the brain what has been already very successfully applied to the spinal cord in tabes, it does look as if some more direct means has been given us than the admittedly futile one of using potassium iodide and mercury products with these patients, or the highly empirical treatment with nucleo-proteid fever. It does seem as if now we could look forward to experimental work on some more direct attack on the spirochæta. I feel that Dr. Noguchi has opened a great field of research and moreover he has demonstrated what I would like especially to bring to the attention of the younger workers, he has shown that it is possible to do much good work in a special field like psychiatry even if one should not expect to devote himself permanently to the whole field of psychiatry. It is possible to single out lines of more or less limited work with excellent opportunities for valuable contributions. I hope that many will be as successful as Dr. Noguchi.

DR. J. HOWLAND: As members of the Johns Hopkins Hospital and Medical School, we are grateful to Dr. Flexner for telling us of the brilliant results that he and his co-workers have accomplished. But as physicians, present and prospective, we owe him a debt which we owe to few other men for information concerning one of the most dreaded and disfiguring of diseases. He has taught us much in regard to the propagation of poliomyelitis, much in regard to its pathology and he has indicated to a certain extent how we may avoid it, but he holds out the hope that no one else has held, that we may perhaps prevent and even eventually cure this scourge, for scourge it is. May I, therefore, Dr. Flexner, on behalf of all of us, express to you our very great gratitude and admiration!

Dr. H. M. Thomas: I may perhaps be permitted to second Dr. Howland's remarks from the neurological point of view, even though the studies at the Rockefeller Institute and elsewhere have transferred poliomyelitis from a strictly nervous disease to one of the general infections, under which heading it is now considered in Osler's Practice. However, as its manifestations are largely nervous, its study falls within my department, and ever since Dr. Flexner and his associates have been announcing at short intervals their many discoveries in regard to it, it has been, I think, the most interesting subject of the course. They have told us much, but there is much left to be made clear, but now that it seems certain that the virus itself has been isolated and cultivated, we await with admiration and confidence still more advance in our knowledge of the disease.

Dr. L. F. Barker: It is a great pity that Prof. Wilhelm Erb, of Heidelberg, cannot be here on this occasion. He has always maintained that tabes dorsalis and dementia paralytica are true syphilitic diseases, and Dr. H. M. Thomas, our neurologist here, has always held the same view. I am told that when Professor Erb heard of Dr. Noguchi's discovery he threw up his hands and said, "Hurrah, hurrah, the proof has at last been brought." Would also that the late Professor Rudolph Virchow could be here. He had always assented to the idea that lues might be responsible, but he insisted that the proof had never been brought. To say that one disease is due to some disease which preceded simply because of this precedence is no very valuable proof. Virchow pointed out that while tabes and general paresis follow lues, they also follow a common cold, for no patient with tabes or general paresis has a history of freedom from common colds! Virchow was right, of course, in pointing to the danger of fallacy; but the clinical evidence in favor of the luetic origin of the two diseases was strong. Could he be here, to-night, he would, I believe, also throw up his hands and rejoice at this demonstration.

America may well feel proud that this finding of the treponema pallidum in the cerebral cortex in general paresis has been made in this country. Of all contributions to knowledge bearing upon psychiatry thus far made in America, it may reasonably be asserted that this one made by Dr. Noguchi is the most important. It is interesting to note that this discovery has not been made by a psychiatrist, but by a man working in a pathological laboratory, one relatively unfamiliar perhaps with the facts of clinical psychiatry. The discovery is of fundamental importance, though, of course, as Dr. Noguchi has said, it does not solve the whole problem, even on the etiological side, though it does open up the way for further research.

The work which was done by clinicians long before the causal micro-organsim of syphilis was known and long before the Wassermann test was devised was really very wonderful. The clinical recognition of a whole series of different types of lues—primary, secondary, and tertiary, and of the paraluetic diseases is what I have in mind. It is the establishment of such syndromes by clinicians that gives the stimulus to laboratory workers for their researches. The fact, now definitely established, that the virus of syphilis is present in the cerebral tissue of paretics does not conflict with the clinical fact that dementia paralytica differs from ordinary cerebral lues. We must still believe that "parasyphilis" differs from "tertiary" syphilis; and we have still to explain the differences. Why does lues affect the cerebrum sometimes in one way, sometimes in another? Are the parasyphilitic diseases due to the arrival of the treponema in areas beyond the blood vessels and the meninges, that is to say, in the tissues of the brain itself? Is it possible that "ordinary" cerebrospinal lues is predominantly an arterial or a meningeal localization of the treponemal injury, and that dementia paralytica and tabes are evidences of predominantly intraneural localization? May we not hope that the demonstration of this peculiar localization of the treponema may lead to a more satisfactory therapy in the paraluetic processes? We have now to find out how to get salvarsan and mercury into spirillocidal relations with the parasites in these relatively inaccessible areas. We have long known that mercury, applied in the ordinary way, though it may help a paraluetic patient, too often fails to arrest the disease; we have had the same experience with arsenic. The stimulating paper read the other night at this Society describing the work of Swift and Ellis on the treatment of paralues excites the hope that a new therapy is being devised that will be far more efficacious than any hitherto available. And it is interesting that the route chosen for the application here is the same as that utilized by Dr. Flexner for the introduction of the curative serum in epidemic cerebrospinal meningitis.

BOOKS RECEIVED.

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